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Virchow's Congenital Encephalomyelitis of the Newborn

Ph. Schwartz, M.D.

Prophylaxis for Foot Eversion in Infants

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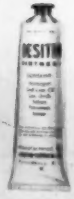

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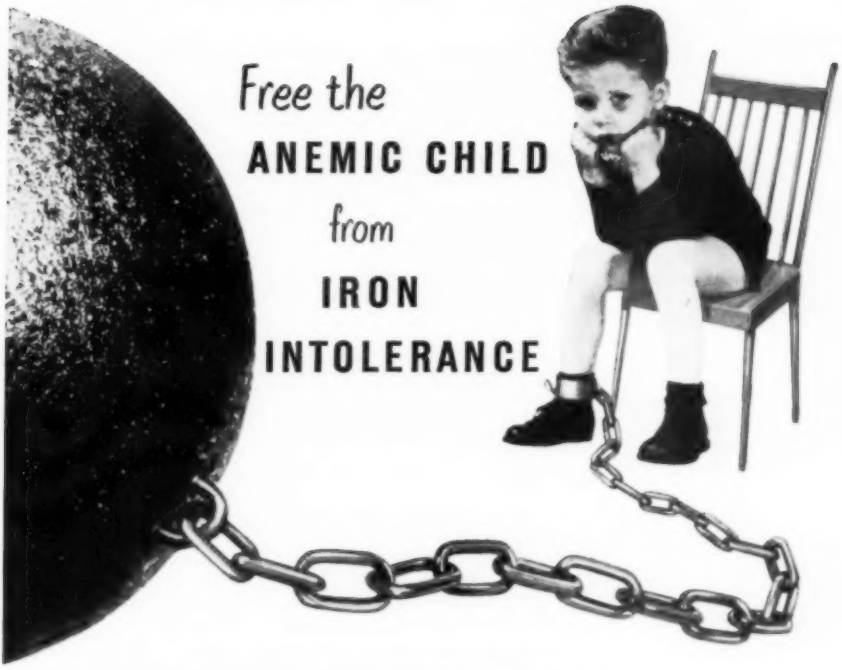

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ARCHIVES OF PEDIATRICS

Vol. 75 MAY 1958 No. 5

VIRCHOW'S CONGENITAL ENCEPHALOMYELITIS OF THE NEWBORN

A Basic but Neglected Problem

PH. SCHWARTZ, M.D.*
Warren, Pa.

I. HISTORICAL REVIEW

In 1920, when the author, in systematic investigations, observed the high frequency of birth traumatic circulatory disturbances in the brains of newborn infants, the next logical step seemed to be the defining of degenerative and disintegrative processes which, in similar conditions, are always present in the brains of adults. The result of this endeavor was the observation of *diffuse and circumscribed softening processes in the brains of newly born children*, characterized by the accumulation of fat droplets in glia cells, and in their derivative elements; *fragmentation of nerve fibers, disintegration of the nervous substance in general*, and *reactive*—regressive and progressive—*changes of the glia cells*, (Figs. 1, 2, 3), just as in adults suffering from primary circulatory disturbances. The knowledge of these microscopic changes of the cerebral substances soon enabled us to recognize the disease with the naked eye: a diffuse, slightly pinkish-greyish discoloration and a hint of a gelatinous consistency of the cerebral white matter, (Figs. 4, 5, 6), indicated the presence of a diffuse rarefaction of the nervous substance (Fig. 7), while small, whitish, opaque spots, (Figs. 4, 5, 10), often located subependimally, corresponded to the circumscribed lesions (Figs. 8, 9). The surprisingly large number of cases of this kind which we collected within a few weeks, convinced us that we were dealing with one of the most common occurrences in pathology. Indeed, these macroscopically visible foci were present in almost every child who survived birth by at least 24 hours, but

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died before reaching the 30th day of life!* We felt it was impossible that we should have been the first to have observed these changes! Thus, began the author's search for predecessors; in Volume 38 of Virchow's Archive, published in 1867, the quest was rewarded when the description of a "Congenital Encephalitis and Myelitis" was found, written by the Master himself. Virchow, the founder of neuropathology, discoverer of the normal glia cells and their pathological transformation in diseased adults, the keen observer, who was the first to see fragmented nerve fibers, found all the changes he knew from his previous studies of adults, present in the brains of infants who had expired before, during, and soon after birth.

According to Virchow, a "fatty metamorphosis" of the neuroglia cells occurred; these elements enlarged considerably during this process and, accumulating more and more fine fat droplets, eventually transformed into large round "droplet cells" ("Körnchenzellen"). If the metamorphosis reached high grades, Virchow related, the round cell disintegrated and eventually no more than a roundish conglomerate of fat droplets remained without being enveloped in a cell membrane. In the cases of "congenital encephalitis" investigated by Virchow, fatty droplet cells affected primarily the cerebral white matter, while the grey substance of the central nervous system showed either no disease, or only changes of secondary importance. As Virchow already observed, the process also involved the columns of the spinal cord. In instances in which the fat droplets gathered in extraordinarily large numbers, whitish, opaque or yellowish-white, dull spots developed, discernible to the naked eye. These foci may be, according to Virchow, minuscule and just at the limit of visibility. However, in some cases macroscopic foci grew to considerable dimensions; often they were not sharply limited, but displayed irregularly jagged, more or less undefined borders. A change in the consistency of the cerebral white matter developed only when the nervous parenchyma also became involved. These softening processes, due to the "congenital encephalitis" according to Virchow, occur rather infrequently, but may transform the whole interior of both cerebral hemispheres into a soft, pulpy mass, in which, microscopically, sometimes shorter and other times longer, slim or thick, spindle-like or club shaped bodies, that is diseased nerve fibers, prevail. No doubt,—according to Virchow—the "congenital encephalitis" may involve the nervous parenchyma itself, disorganizing its function and destroying the life of the victim. Virchow observed that the disease may be accompanied by extreme "apoplectic" hyperemia, which he considered the consequence of glial changes in the nervous tissue. Also, he felt that an enlargement and even proliferation of the glia cells occur before the fatty metamorphosis begins. He spoke of an "interstitial" disease, because of the predominance of glial changes initiating the condition. Virchow emphasized the great practical importance of his discovery with the following statement: "Many children die after birth of atrophy, or diarrhea—it is said—and the autopsy discloses a diffuse encephalitis of the cerebral white matter."

All these observations were made during a smallpox epidemic in Berlin. It seemed to Virchow, that "encephalitis" occurred

* We may cite here Aschoff's statement (1925) confirming our observations: "The autopsy of each newborn child who survived for some days, disclosed smaller or larger softening foci as being the consequence of birth trauma. The frequency of birth traumatic lesions is surprisingly high."

especially often in newborn children of mothers suffering from smallpox or syphilis. Although the infants displayed no cutaneous eruptions, characteristic of smallpox, Virchow believed that the cerebral changes he observed in the newborn could be compared with changes in other organs—for example: kidney and liver—which generally accompany acute exanthematous conditions in adults.*

In instances in which the "interstitial encephalitis" accompanies congenital syphilis, macroscopic brain foci may be, according to Virchow, compared with miliary gummatous nodules of the liver. Also, he compared the diffuse type of "encephalitis" with syphilitic interstitial nephritis—a disease in which the fatty "metamorphosis" (degeneration) of the renal connective tissue sometimes reaches a degree of such intensity that the yellow spots of the involvement become visible to the naked eye. No doubt, these observations on renal pathology have had a profound influence on Virchow's concept concerning the "congenital interstitial encephalitis". Virchow felt, nevertheless, that the etiologic factors mentioned did not suffice as an explanation of every case of "congenital encephalitis". He even stressed that in some of the investigated instances, there was no maternal disease the transmission of which to the child could be assumed.

Virchow's publication almost immediately received general acceptance (v. Grafe; Hirschberg). As early as 1868, it seemed evident that the newly discovered disease was of greatest importance as the explanation of the infant mortality. Hayem, in Paris, immediately after the publication of Virchow's paper, investigated about a dozen newly born infants, and reported that he was able to observe in each case various degrees of the cerebral changes described by Virchow. This, perhaps too acquiescent, endorsement prompted Virchow to stress that the fatty "metamorphosis" did not occur in every stillborn child, or in all children dying subsequent to birth; of course scattered fatty "droplet-cells" do not count and fatty deposits appearing in perivascular spaces and in capillary walls are not always connected with "encephalitis." Incidentally, Hayem rejected the infectious origin of the disease and was soon supported by Parrot, who believed that the changes discovered by Virchow indicated a primary fatty degeneration of the glia cells—mainly induced by defective nutrition, an "athrépsie" affecting the whole body. At any rate, both Hayem and Parrot assumed that the condition discovered by Virchow was of pathological nature.

Jastrowitz, recognizing the basic importance of Virchow's observations in neuropathology and pediatrics, intended to investi-

* In our day "inflammation" especially "encephalitis" is considered almost synonymous with "infection". Not so in the period of Virchow's discovery. Virchow named the condition "encephalitis" only because he felt that its morphological aspect corresponded to the definition he gave inflammatory processes.

gate the clinical symptomatology of the new disease; therefore, he first collected brains of infants who, before death, had disclosed signs of brain lesions. In all these cases the changes described by Virchow were present without exception. Also, those periventricular, yellowish, opaque spots, considered by Virchow to be macroscopic foci of "congenital encephalitis," were found frequently by Jastrowitz. At first it seemed quite clear that all these findings were linked with symptoms observed clinically. However, Jastrowitz soon became less certain and suspected that the fatty inclusions in glia cells were not of pathological significance, but

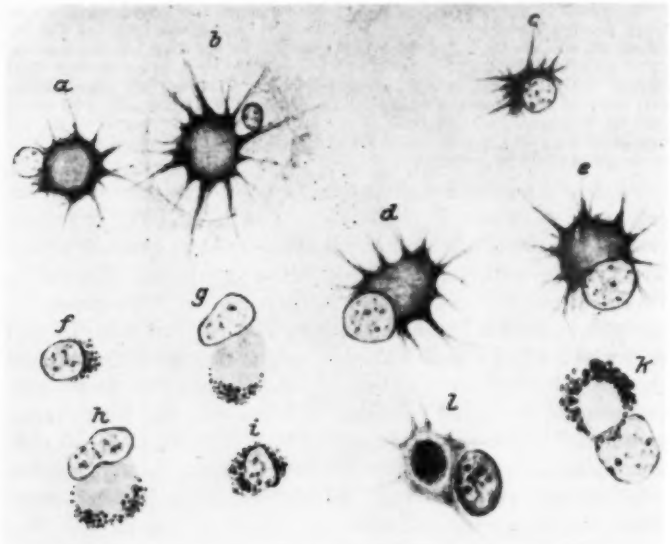

Fig. 1. Glia cells in the brain of a newborn. (*c*) Normal astrocyte. (Alzheimer-Mallory staining). (*a*), (*b*), (*d*) and (*e*) Hypertrophic glia cells. (Alzheimer-Mallory staining). The cytoplasm of these cells appears enlarged. The processes are clearly seen. A central portion of the cytoplasm shows special staining. The same portion of the cytoplasm appears in the shape of a ball if Alzheimer-Mann staining is used (*l*).

(*l*) In this cell, a narrow, ring-shaped space is visible between the peripheric and central area of the cytoplasm. Staining with scarlet red shows that the ring-shaped space contains fat granuli. (*f*) and (*i*) Glia cells with normal sized cytoplasm containing fatty deposits. (Scarlet red staining). (*g*), (*h*) and (*k*) Glia cells with hypertrophic cytoplasm containing fatty deposits. (Scarlet red staining).

These types of glia cells are present in all kinds of fresh lesions of the brain tissue in adults, too. Cells containing fat which we show in these figures were designated by Merzbacher as pathological elements of the brain in newborn children; Wohlwill considered them physiological.

probably were related to the normal development of the myelin sheaths.

Another of Jastrowitz's remarkable observations is the following: Infants, displaying clinical cerebral symptoms, and showing at autopsy glial "metamorphosis," often had been subjected to a birth process of long duration; he stressed that the heads of these children were exposed to prolonged mechanical injuries and circulatory disturbances; he recalled cerebral hemorrhages in the newborn described by Cruveilhier which in Jastrowitz's opinion easily could have induced "consecutive softening" of the brain substance. Also, it merits mentioning, that after 14 years—having investigated a total of one hundred and sixty corresponding cases—when Jastrowitz once again summarized his views, not one of his old arguments (always introduced by "perhaps," "probably," or "assumedly") became established truth!

The present day history of medicine disregards, in general, the psychological conditions which may explain the discovery and the general acceptance of new facts—or their neglect. However, the development of our knowledge concerning Virchow's discovery cannot be understood without considering certain facts of psychological impact. On the one side we see Virchow, the dominant personality in medicine, at the peak of his research activities and his fame, announcing that he had discovered one of the most important causes of human loss and suffering; and on the other side, a young man at the beginning of his career, claiming that the newly discovered changes are only of importance insofar as they accompany a normal developmental process. And, nevertheless, in this disproportionate struggle, it did seem for decades as though Virchow was the loser. This fact strikes us the more forcibly, inasmuch as Jastrowitz considered all cases to be diseased in which fatty metamorphosis of the glia cells appeared in macroscopic foci of the cerebral white matter, or, when it was visible, even though only microscopically, in the cerebral cortex, in the basal ganglia, etc. Also, he admitted that he could not find criteria which would enable him to differentiate between the intensely diffuse fatty infiltration of glia cells, which he too considered pathologically significant, and those slighter fatty deposits, occurring "normally".

Why has not Virchow upheld his teaching more energetically? Why did he—he, who lived, searched and taught for 30 years after Jastrowitz's rebuttal—permit the entire problem to sink into oblivion? Was he impressed by the arguments of his opponent? Was he too preoccupied with his political activities? Remember, this is the period in which his greatest parliamentary adversary, Bismarck, destroyed the French army, unified the German Reich and silenced all opposition. It is also at this time that Virchow's ablest pupil, Cohnheim, proved that the inflammatory cells originate in the blood and are not products of the transformation of connective tissue elements, as the Master maintained. And this is the period, too, in which Virchow suffered his greatest scientific defeat, when, against his unrelenting opposition, it was shown that tuberculosis is an infectious disease, and that miliary tuberculosis, pulmonary phthisis, as well as scrofulosis, are caused by the same living agent. In 1883, he once again repeated his arguments published in 1867, upholding his original statements without trying to refute adverse comments. He had not cared to investigate in the meantime the frequency of macroscopic foci, the pathological significance of which was generally accepted, and which are almost always present in children who survive their birth, yet die before the thirtieth day of life. He neglected to consider the

connection between fatty glial deposits and the development of the myelin sheaths, which today is known to be non-existent, and he ignored Jastrowitz's suggestion that mechanical injuries and circulatory disturbances, suffered during the birth process, could be of importance in the causation of the cerebral softening processes. Also, in this last discussion, he forgot to emphasize that the fatty metamorphosis of the glia is only one of the signs of a disease in the central nervous system of the newborn, accompanying lesions of the nerve fibers and paralleled by the proliferation as well as decay of glia cells, facts, which he stressed in his first descriptions. Virchow's main argument remained the same as in his previous publications, namely, that cases occur in which no fatty metamorphosis of the glia can be detected, and that, therefore, brains in which the fatty "metamorphosis" is present, are to be considered as diseased.

Virchow, as well as Jastrowitz, performed his investigations with the help of unstained specimens which were prepared by teasing the brain tissue with steel needles; or by inspecting rather thick unstained sections microscopically. Our present day routine methods of frozen sections and the staining of fat substances were unknown at that time. In retrospect, we may admire the manifold observations Virchow was able to make with the primitive means then available. Also, based on our own experience, we may state that Jastrowitz, if he had been consistent in his opinions, would have declared even more cases to be diseased, than did Virchow himself.

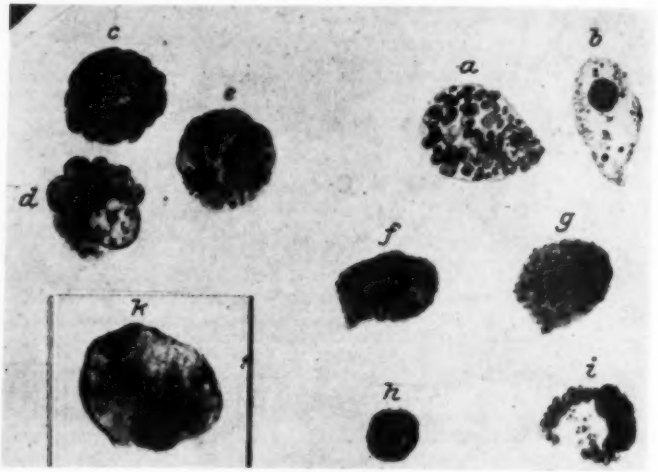

Fig. 2. Fatty scavenger cells in the brain of infants of various ages. (Scarlet red staining). (*a*) and (*b*) Cells from the marginal area of a softening focus in a 2-day-old child. (*c*), (*d*) and (*e*) Fat-laden glia cells from the border area of a birth traumatic focus in a 6-day-old child. (*e*) This scavenger cell is filled with nuclear fragments. (*f*) and (*g*) Scavenger cells from a 20-day-old and (*h*) from a 3-month-old softening focus. (*i*) Disintegrating, fat-containing scavenger cells. (*k*) Young scavenger cell stained by *Alzheimer-Mann* method.

These cells were designated by Merzbacher as physiological elements of the brain in the newborn infant. (Merzbacher has never seen softening foci in the brain of newborn infants as described by Virchow and Parrot and shown in Figs. 4, 5, 8, 9). Wohlwill supposed the same cells to be pathological. These cells characterize all kinds of acute and subacute cerebral softening processes in adults.

If we disregard two publications—Limbeck's in 1886, and Fischl's in 1899—which dealt with cases of the "congenital interstitial encephalitis," characterized by extensive cerebral destruction, we find absolute silence on these problems for decades. In 1900, Thiemich, employing the osmium staining method, tried to revive the discussion claiming that Virchow was right. He did not succeed; neither did Merzbacher who, in 1907, with the help of more modern methods reviewed the entire problem. A dogma was proclaimed and generally accepted: *Fatty deposits in glia cells of the brain in newborn children are of physiological significance and linked, in some way, to the development of myelin sheaths; and, that these changes have no real pathological importance.* The impression made by these assumptions was so profound that the problem of Virchow's "congenital encephalitis" was never mentioned in text books of pathology, pediatrics, nor neurology. Even large handbooks of neurology and psychiatry omitted mention of these findings and discussions, although dwelling at great length on hypotheses explaining fetal cerebral diseases and congenital conditions such as Little's disease, athetosis, feeble-mindedness and epilepsy.*

Merzbacher, in 1907, employing modern section and staining methods discerned two types of fatty glia cells in the brains of the newborn: (1) round elements, resembling genuine phagocytes —which he assumed were physiological elements transporting fatty substances for the development of myelin sheaths, (Fig. 2); (2) fatty glia cells with extensions, anchored within the nervous substance, indicating—according to Merzbacher—a morbid condition, (Fig. 1). We do not wish to relate here the rather tortuous path of reasoning which led to the formation of Merzbacher's opinion. At any rate, Merzbacher emphasized that the elements he considered signifying pathological conditions were present in the majority of cases investigated by him. Fourteen years later, in 1921, Wohlwill considered the fat containing glia cells having extensions to the physiological and regarded the round elements—which Merzbacher described as physiological—as pathologically significant.

Wohlwill accepted as a proven fact that glia cells containing fat droplets occur normally, and that these elements are of importance in the development of the myelin sheaths. He investigated three cases in which periventricular hemorrhage, thrombosis, or softening was present, and assumed that the fat containing elements in these foci could be safely regarded as

* It seems that a change is occurring in this attitude at present. In the Handbuch der speziellen pathologischen Anatomie (Handbook of Special Pathological Anatomy), Vol. 13, part 3, 1955, Siegmund reported in a comprehensive review on Virchow's "congenital encephalitis" confirming the results of the present writer and declaring the changes to be mainly caused by birth injuries.

pathological. The roundish fat droplet cells he found in this area were identical to scavenger ("gitter") cells in analogous processes occurring in adults (see Fig. 2). Wohlwill was well aware that fat containing star-like glia cells, or fatty spider cells—which, observed in the brains of newborn children, he assumed to be normal—occur in diseased cerebral areas of adults (see Fig. 1). Therefore, he considered that this type of fatty glia cell in the brains of newborn children also may indicate pathological processes.

All these attempts to differentiate between "normal" and "pathological" fat containing glia cells have no true practical value, because generally both types of cells occur together. Merzbacher, therefore, could by a strict application of his criteria designate the same number of cases as being pathological as could Wohlwill, in spite of the fact that Merzbacher considered Wohlwill's physiological elements to be of pathological significance. On the other hand, both Merzbacher and Wohlwill would have to accept the same incidence of pathological cases as Virchow claimed—he who considered all fatty glia cells as signifying disease!

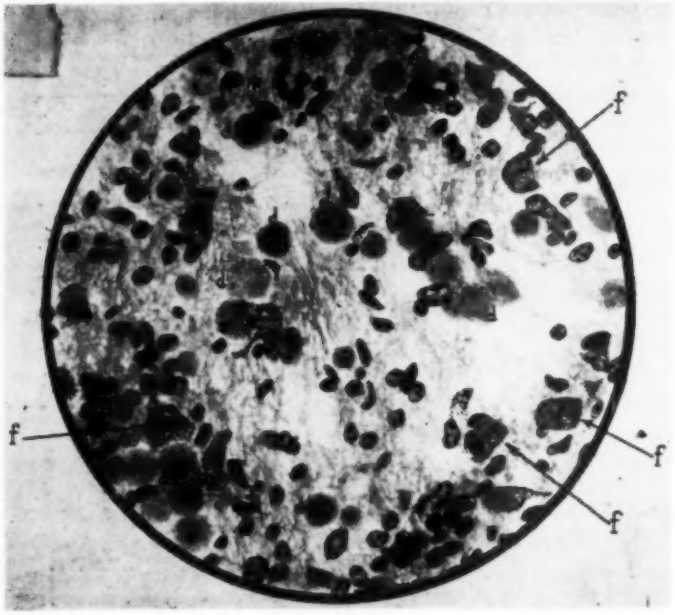

Fig. 3. Marginal area of a birth traumatic cerebral softening focus in a 3-day-old child. Numerous fat containing cells. (*f*) Round nucleated debris, (*d*) of fragmented nerve fibrils.

Ceelen (1920-1921) expressed his inclination to consider the diffuse fatty glial deposits as physiological. However, he declared almost every case he investigated was affected by disease because

he—nota bene, mistakenly—regarded certain cellular agglomerations in the brain of the newborn as of inflammatory origin.*

Ceelen's associate, Gohrbandt (1923), followed his teacher in considering the diffuse glial fatty deposits as normal. However, he remarked that "sometimes the number of fatty glial elements appears to be so enormous that it becomes impossible to free the observer from the idea that a pathological process is present". According to Gohrbandt, "in facing the problem of the diffuse glial deposits, the situation was so complicated and the interpretation of the observed changes so difficult, that there is not a possibility of arriving at a definitive explanation." Gohrbandt tried Wohlwill's criteria, but found them unsuitable for the purpose of differentiating between physiological and pathological processes, "as frequently a combination of both occur, making it difficult to tell what is normal and what is not."**

Reviewing all the investigations and results related to the significance of fatty glial cells in the central nervous system of newborn children, we may state that the occurrence of every type of these elements was considered both normal and pathological. There is no one investigator of these problems who definitely declared a certain type of fatty glial deposits in the central nervous system of the newborn to be normal; and there exists no type of fatty deposits in the central nervous system of the newborn, the pathological significance of which has been definitely denied. This clinging to traditional concepts always has produced the same type of results: The various authors—believing that one or the other of the phenomena observed could be helpful in discriminating between pathological changes and normal processes—always arrived at the same indeterminate conclusions.

And, if we ask why investigations performed with the help of abundant human and animal materials, always resulted in doubtful and ambiguous statements, then we may assume that it was because, apparently the "fatty metamorphosis" of the glia, discovered by Virchow—to be either normal, or pathological—had no real practical medical significance.

In this sense, we were fortunate to have first observed the manifold types of cerebral injuries in newly born children, and to have been induced by these new facts to look for the inevitable subsequent changes of the nerve substance.

---

* Ceelen encountered in the brain of the newborn, groups of matrix cells located subependymally and showing a tendency to perivascular arrangements. He believed these cells to be lymphocytes. His interpretation of the diffuse fatty deposits appear the more astonishing when we recall that he noted 23 instances in which cerebral softening foci were present—a characteristic, known today, of birth traumatic lesions.

** Gohrbandt reported on sixteen infants showing macroscopic cerebral softening foci.

II. NEW INVESTIGATIONS

In spite of the confusingly vague and contradictory observations, what caused the rejection of Virchow's teaching to become almost traditional? We believe that the following factors were responsible: (1) the comparison and identification of observations in animals with the results of investigations in human pathology; (2) the assumption of a connection between glial fatty deposits in newborn children, and the development of myelin sheaths; (3) the incomplete description of conditions present in the central nervous system of the newborn; and, particularly, (4) the lack of demonstrable and obvious pathogenic influences which could explain, authentically, the processes interpreted by Virchow as pathological.

ON THE OCCURRENCE OF CELLS IN THE CENTRAL NERVOUS SYSTEM OF DEVELOPING ANIMALS CONTAINING FATTY INCLUSIONS

Jastrowitz already believed he had seen changes in animals which confirmed his concepts on the physiological nature of fatty glia cells in the brain of the newborn. Boll, Eichhorst, Wlassak, Schröder and Merzbacher, from their own investigations on animals, arrived at the same conclusions. However, the factual observations of these authors are contradictory, nebulous, and often mistaken—having naught in common with Virchow's observations concerning the brain of the newborn. In extensive systematic investigations performed by the author on fifty fetuses of slaughtered bovines, representing every degree of development from the third fetal month to maturity, it was found that only scattered fat containing cells occur in the central nervous system of cattle during the entire intra-uterine development, and, that they are restricted to the vascular adventitial sheaths and to the covering membranes of the brain and the spinal cord. The same is true of fetuses of cats, dogs, swine, goats, mice, rabbits, also chicken and geese. [Staemmler, 1923; Siegmund, 1922-1923; Berberich and Bär, 1925; Brunner, 1928].*

We showed that all types of fatty glia cells, in circumscribed

* Berberich and Bär employed not only the usual Scarlet-red and Sudan staining, but also searched for inclusions demonstrable by the methods of Lorrain-Smith, Fischler and Smith-Dietrich. These authors combined all methods mentioned with Hortega's impregnation, as Hortega claimed that the elements he discovered were, during embryonal life, identical to Virchow's fatty droplet-cells in the brains of newborn children: "Hortega cells, under normal conditions, contain no fatty inclusions." (Berberich and Bär, 1 c).

foci and scattered diffusely, appeared in every case in which a newborn animal suffered a suitable experimental lesion. Berberich and Bär confirmed these observations. They found that fat droplets appear in Hortega cells after an injury of newly born animals. We assume that the question whether the normal cerebral substance of fetal and newborn animals display findings which may be compared, or identified, with fatty deposits observed in newborn children, can be considered as definitely answered. *There exist no similar changes normally.*

ON THE RELATIONSHIP BETWEEN THE DEVELOPMENT OF MYELIN AND THE PRESENCE OF GLIA CELLS DISPLAYING FATTY DEPOSITS

It occurred to Jastrowitz to link the fatty glial deposits discovered by Virchow with the development of the myelin sheaths. This idea returned later in some form in every publication dealing with the fatty deposits in the brains of newborn children. Every investigator formed his own theory concerning this connection, but not one neglected to emphasize that he was elaborating on a purely hypothetical basis! In spite of these facts, the construction of a connection between fatty glia cells of the central nervous system and the development of myelin sheaths became almost axiomatic and so deeply rooted that it was used as the self-evident starting point for scientific research.

The course and arrangement of the various tracts of nerve fibers which, in the brains of adults, are characterized by myelinization, are discernible in the early stages of fetal development—long before a typical Weigert staining can be achieved in the same cerebral region. The tracts appear as closed entities, surrounded by nerve bundles going in other directions, and by nests of embryonal nerve cells. Between the parallel fibers of these tracts and bundles, germ cells and glia cells are present, defining an inner texture of the complex, which resembles mature structures in adults. Thus, the inner organization of a certain tract, the relationship between glia cells and nerve fibers—even the form of the mature system—show only slight alterations during the development, while the composition of the substances enveloping the nerve fibers, and the extension of the nerve fibers, changes. The nerve tracts and the individual nerve fibers become, together with the growing organism, thicker and longer; at the same time, the myelin sheaths arrive at maturity. Indeed, the perfect Weigert staining indicates a certain degree in the maturation of the myelin sheaths. However, a nerve fiber can be considered as definitely mature only if it reaches its maximal extension and thickness by the close of the organism's period of growth. Thus, should we intend to link the myelinization to fat containing glia cells, we would, perhaps, have to show the occurrence of these elements up to the conclusion of the development of the nerve fibers. However, no one has seen anything like this, and there were none who claimed its existence.

Westphal (1894, 1897) emphasized that the myelinization of peripheral nerves develops independently of fat-containing cells.

The fact that Virchow's fatty glia cells are not present in the

normally developing brain of animals, mentioned before, implies that the myelinization, in this case, occurs without their assistance. As basic embryonic developmental processes are identical in the various species, it is a priori improbable that the development of myelin sheaths in man can be linked to the presence of fatty glial elements.

Nevertheless, we found it essential to investigate the myelinization in the human central nervous system itself. We began by following the myelinization in the *pons*, a part of the brain which, in newborn children, only rarely contains fatty glia cells—even in cases in which the cerebral white matter appears to be affected most intensely. We investigated fifty cases including every stage of development, from a 25 cm. long fetus, up to adult persons. There can be no doubt about the fact that the normal myelinization in man occurs in the pons without any interference from fatty glia cells. This should suffice to characterize the development of the myelin sheaths of the entire nervous system, because Flechsig's dictum: "the myelinization in every part of the organism de-

Fig. 4. Fresh necroses in the cerebral white matter in a 2-day-old, full term child. The necroses are located in the area supplied by the terminal vein. Arrows: Fresh necroses of the cerebral white matter; (*t*) thalamus; (*p*) putamen; (*e*) intense hyperemia and gelatinous edema of the brain substance, indicating diffuse fatty degeneration of the glia.

velops in the same way" still is generally accepted. However, we investigated the *medulla oblongata* as well. In the relatively few newborn children who displayed fatty glia cells in this part of the brain, these elements signified secondary degeneration, following extensive lesions of the entire brain, or appeared subsequent to circumscribed local lesions. Fatty glia cells are of relative infrequence in the *basal ganglia*. For every case in our material in which these brain parts displayed fatty elements, we have been able to cite a great number of other instances of the same developmental stages, in which no traces of fatty deposits could be detected. No doubt, the normal myelinization of the basal ganglia occurs independent of fatty glia cells. The independence of the myelinization in the *cerebral cortex* from fatty glia cells can be easily shown: In the great majority of cases no fatty glia cells occur in the cortex, and the exceptional instances in which glia cells do contain fat droplets can be compared with many cases of the same developmental stages showing no trace of fatty deposits. No doubt, the normal development of the cerebral cortex has nothing to do with fatty glial elements. The same is true of the gray matter of the spinal cord — as is easy to prove. Thus, it remains to show that the development of the *white matter* of the cerebral hemispheres and of the columns of the spinal cord is also independent of the presence of fatty glia cells. In endeavoring to prove this statement, we prefer not to make use of Flechsig's axiom considering myelinization to be the same in all parts of the organism. Also, we refrain from relying on the observation that in animals the myelin sheaths of the cerebral white matter develop just as in all other parts of the central nervous system — a fact which would seem to imply that differences cannot be present in the human species either. In reality, fatty glia cells occur so frequently in the cerebral white matter, that it is quite understandable why so many investigators were unable to free themselves from the impression of this phenomenon being normal.

What is the significance of these findings in the cerebral white matter? Can there possibly be a connection with the normal myelinization? If we should concede such a connection in this part of the central nervous system, we would then be forced to make a number of rather peculiar assertions: (1). The admission that not only the myelinization of functionally different parts of the central nervous system proceeds differently, but that the fibers of the same structural and functional entity, for example, of the pyramidal tract, develop differently while passing through the

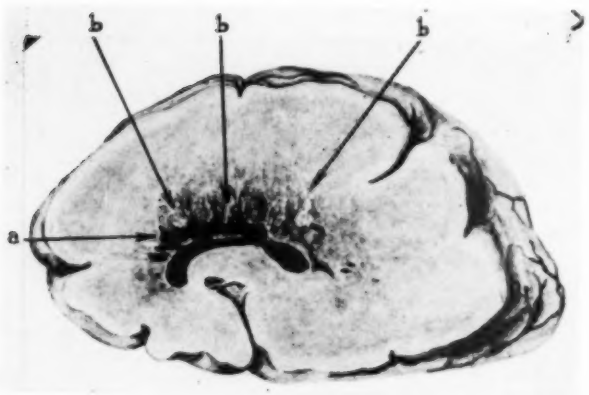

Fig. 5. Strip-like hemorrhages and numerous small softening foci (stained yellow by biliary pigment) in the occipital lobe of a six-day-old premature. The lesion is located in the area supplied by the lateral ventricular vein. a . . . hemorrhage; b . . . softening.

Fig. 6. High-grade hyperemia in the white matter of the frontal lobes of a stillborn premature infant. Microscopic examination showed very numerous capillary hemorrhages, accompanied by rarefaction of the tissue and by diffuse fatty degeneration of the glia cells. (Similar to the case shown in Fig. 13).

cerebral white matter, the internal capsule, the pons, the medulla oblongata, and the spinal cord; (2). We would have to assume that the development of the myelin sheaths, even in areas in which it is dependent on the presence of fatty glia cells, shows variations unprecedented in other developmental processes: it would seem that the myelinization of the corpus callosum or of the subependymal white matter in general needs the particularly intensive assistance of fatty glia cells, while the development of the sub-

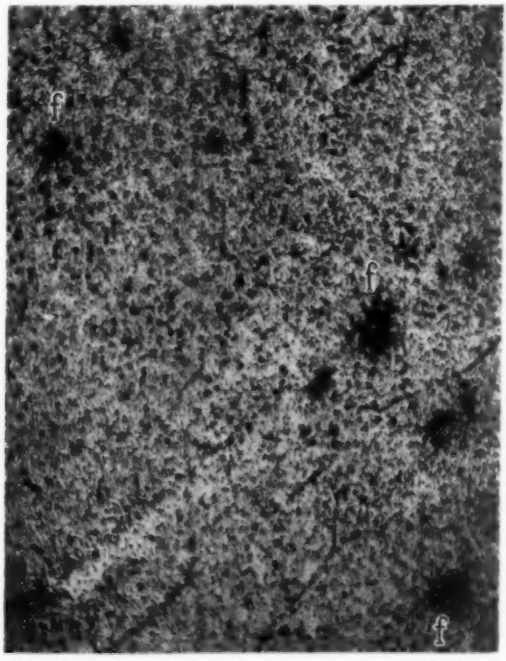

Fig. 7. Diffuse fatty degeneration of glia cells in the cerebral white matter of a full term, 6-day-old child affected by birth trauma. (Fat staining). Microscopic examination disclosed numerous very small softening foci. These findings characterize Virchow's interstitial encephalitis in the newborn. (*f*) Minute softening foci displaying the conglomeration of fatty scavenger cells.

cortical and the central white matter proceeds mostly with the modest intervention of fatty glia cells, and sometimes even without such aid: (3). We would have to agree that the association between myelinization and the presence of fatty glia cells varies, in regard to the duration of time, in the different areas of the cerebral

white matter. Actually, this association persists much longer in those areas — namely, corpus callosum, subendymal white matter — where the fatty glia cells occur in particularly large numbers; while the subcortical white matter — the maturation of which depends on only a few fatty glia cells — shows the presence of these elements for only a very short time; (4). The cerebral white matter of newborn children, very frequently, in a certain region of one hemisphere shows no fatty glia cells, or, only a very few; while the same location in the other hemisphere is characterized by a particularly intense accumulation of these elements. Is it logical to assume in these cases that the myelinization in one cerebral hemisphere proceeds without the assistance of fatty glia cells, and, in the other hemisphere through their intervention? (5). The variability of the amount of fatty glia cells in certain areas of the cerebral white matter astonished all investigators. Siegmund stated the following: "Fluctuations in the extension and intensity of the fatty deposits . . . make it impossible to set embryological standards for the association between myelinization and the presence of fatty glia cells. . . . Investigating the development of certain tracts, no regularity can be shown in regard to timing and quantity in the occurrence of the fatty glia cells." Wohlwill observed similar facts: "Investigating a larger number of children's brains, the great differences in the quantitative findings were astonishing . . . in two children equally developed, the same cerebral area may display in the one case, very intense, and in the other, only scattered fatty glia cells." Also Wohlwill emphasized that fatty glia cells, in general, occur in markedly greater numbers in those children who survive birth at least for a few days, than in stillborn infants, or, in children who die immediately following birth — regardless of whether the children are premature or fully developed. All these observations are in concurrence with our own experiences. The variability of all these findings is amazing indeed, and without comparison in embryology.

Neuburger summarized his observations as follows: "The extension of the areas containing fatty glia cells shows considerable differences, even in equally developed children; in one case, almost the entire cerebral white matter is involved, in another, only the periventricular region, or, there are only scattered, indefinitely circumscribed foci located deep within the white matter." Neuburger too, expressed his astonishment concerning the variability of the findings while investigating a greater number of cases. (6). We see, that the hypothesis concerning the myelinization of the

cerebral white matter, of the corpus callosum and of the cerebral spinal tracts obligatorily being assisted by fatty glia cells, led to rather eccentric assumptions. However, the situation becomes even more difficult when we learn that there are cases of newborn children in whom even the typical locations show *no trace of fatty deposits.*

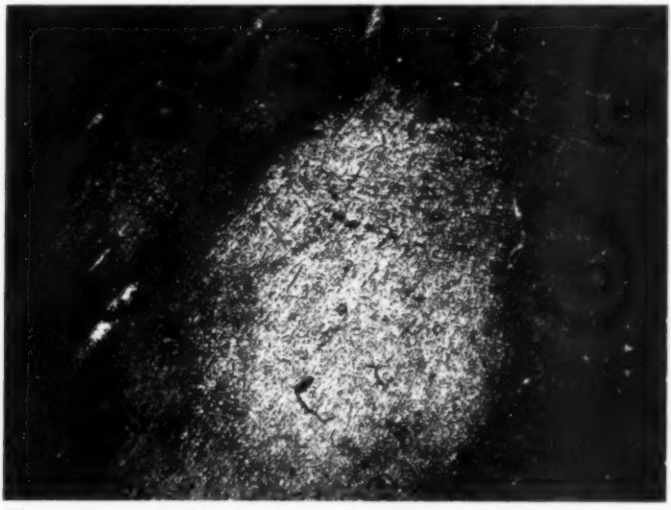

Fig. 8. Circumscribed birth traumatic rarefaction focus located in the periventricular cerebral white matter. A 24-hour, full term baby.

Instances in which no fatty glia cells occurred were observed by Virchow. Of course, Jastrowitz too encountered — though rarely — cases in which no fatty deposits of the glia were present. He did not hesitate to declare that these were the pathological instances!*

Thiemich (1900) investigated a 6-week-old child in whose brain no trace of fatty deposits could be found. Ceelen (1920-1921) reported on three similar cases. The author himself encountered fifteen instances belonging to this group, in a series of three hundred brain investigations. Siegmund (1923) and Lubarsch (1923) too, emphasized the occurrence of cases in which no fatty

* Thus, Jastrowitz believed he had observed the following pathological conditions in the newborn: 1.) Cases in which macroscopic conglomerates of fatty glia cells were present. 2.) Instances in which the diffuse fatty metamorphosis in the cerebral white matter surpassed a certain degree. 3.) Cases in which the cerebral cortex, the basal ganglia, or the spinal cord, were involved. And finally, quite paradoxically, 4.) Cases in which no fatty metamorphosis of the cerebral tissue could be detected.

glia cells were present. Neuburger (1925) related the case of a 4-month-old infant who — without previous illness — suddenly died; the brain of this child had no fatty deposits, although, as Neuburger emphasized, the brains of other children of the same age or even older displayed many fatty glia cells. According to Neuburger this thoroughly investigated case illustrates once more that the presence of fatty glia cells has no connection with the normal myelinization and is to be considered a pathological phenomenon.

In spite of his observations related to the frequency and intensity of birth traumatic cerebral lesions, Rydberg held that the "appearance of morphologically visible fat in the tissue interstices and on the surface of the glia cells" are normal occurrences. (Rydberg, l. c., p. 60.) It seems that he has not seen any cases, in which fatty glia cells were absent. However, his descriptions and the pictures he used in illustrating his statements—particularly Figs. 27, 28 and 31—reveal clearly enough that substances considered by Rydberg as "fat" are not always the same compounds as those discussed in the publications of Virchow, Merzbacher, Wohlwill, Siegmund and this author, but rather may be compared with those observed in the investigations of Wlassak, Schröder and Boll, having no relation to the problem of Virchow's encephalitis. We have not dealt with undefined substances "in the tissue interstices and on the surface of the glia cells" but investigated deposits of neutral fat *in* glia cells.

(7). If we accept the view that myelinization of the cerebral white matter is linked to the presence of fatty glia cells, then we will also have to agree that the absence of these elements indicates disease. We mentioned that Jastrowitz in the early years of the discussion actually took this position. A modern author, Scheyer, under the guidance of Wohlwill (1924), investigating the development of the spinal cord came to the same conclusion. He found fatty glial cells to be completely missing in the spinal cord of a 22-day-old infant, born prematurely only seven and a half months after conception. Scheyer maintained that the myelinization of the spinal cord columns, in this instance, obviously was retarded, since he was able to compare this case with many other children of the same age and developmental stage, who displayed the fatty deposits.

The conclusion that the absence of fatty glia cells in the cerebral white matter and in the columns of the spinal cord signifies a morbid condition would be — if correct — one of the strangest facts in science, as no one doubts that the presence of these elements in the cerebral cortex, the basal ganglia, the pons and the medulla oblongata means disease.

Scheyer and Wohlwill asserted they had encountered in their investigations of sixty-three cases, only one instance—the above mentioned one—in which no fatty glia cells were present in the developing spinal columns. The author,

however, was able to prove that in reality no less than twenty-three cases of this kind were observed by the other two. Wohlwill graciously admitted his error. Had they not made this strange mistake in accounting their "negative cases", Scheyer and Wohlwill would have refrained, perhaps, from considering, in a group of sixty-three observations no less than twenty-three cases as diseased because of the absence of fatty glia cells.

Gröntoft recently reported on the following observations: In a group of twelve infants who died shortly before or immediately after birth, two children (weights, 880 grams and 4,650 grams, respectively) showed no fatty glial cells. Rough traumatic cranial lesions occurred in six cases; Penfield's silver impregnation showed a degenerative change of the neuroglia in every case, and also, microscopic hemorrhages of cerebral parenchyma were present in every instance. (Tables 15 and 16 of Gröntoft's paper).

In another group of ten newborn children with a birth weight of 540 to 2610 grams, who died after prolonged asphyxia ("anoxia"), every case disclosed degenerative changes of the neuroglia cells and microscopic hemorrhages of the cerebral parenchyma, while fatty glial cells were present only in one instance (a premature child weighing 1190 grams).

In a third group containing eight fetuses (weights from 520 grams to 2700 grams), Penfield's silver impregnation disclosed degenerative changes of the neuroglia in every case, and also, microscopic hemorrhages were present in each instance. However, glia cells containing fat granules were found in only five cases. We refer to these observations, yet we would stress that the number of cases in which *no* fatty glia cells were found, in Gröntoft's material, is much higher than in our own observations.

(8). We mentioned that macroscopic necroses and softening foci of the cerebral white matter are a rather common occurrence. In these foci, (Figs. 4, 5, 9, 10), the pathological nature of which cannot be denied, the same types of fatty glia cells appear that characterize the areas in which the controversial diffuse fatty deposits are present. Thus, we face one more paradox: If we decide to follow Merzbacher, we will have to accept the same round fatty glia cells (Fig. 2.), occurring "normally" in the areas of diffuse fatty deposits as indicative of disease in the circumscribed micro- and macroscopic foci. On the other hand, if we follow Wohlwill, we will have to consider the fatty glia cells displaying extensions, (Fig. 1) when observed in macroscopic softening foci, as a sign of decay and disintegration; while, when occurring in regions of the diffuse fatty deposits, as signifying normal processes directed toward building up myelin sheaths.

Scientific progress is not possible without discussion. In this sense the author was fortunate enough to have had two eminent adversaries, on the subject of Virchow's encephalitis. One of them, Siegmund, soon became fully convinced, generously confirming the observations and views of the author. Wohlwill's attitude seems still indefinite; while on the one hand, confirming the author's findings relative to the frequency, morphology, pathogenesis and social implications of the birth traumatic cerebral lesions in newborn children, his position remained rather ambigu-

ous on the question of the fatty glial deposits. In an article published in 1936, Wohlwill interpreted this writer's results as follows: "If Schwartz were right then it should be concluded that more than half of humanity suffers cerebral lesions through the birth process" . . . "should we say that humanity, to date, remains backward in development because almost everyone has received a blow at birth?" (Wohlwill, l.c., p. 50).

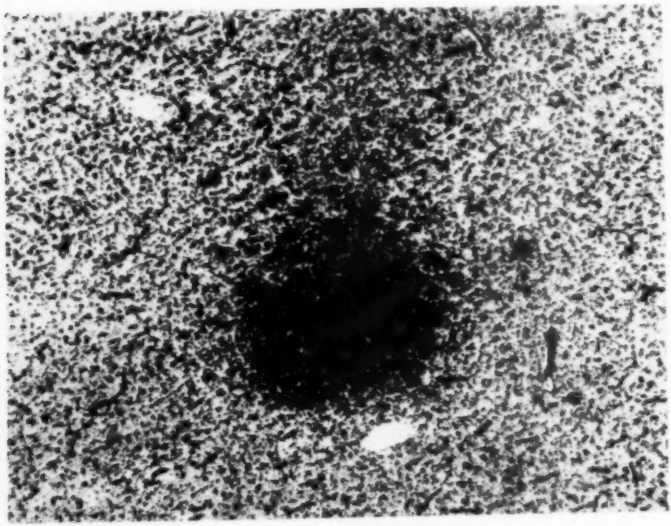

Fig. 9. Birth traumatic softening focus of the frontal cerebral white matter in an 8-day-old child of full term birth. The black conglomerates and spots represent glia cells containing fat droplets, stained with scarlet red. The central focus was just visible macroscopically. The environment of this focus displayed a marked rarefaction process characterized by the disappearance of the basic glial substance; in this area many round scavenger cells and star-like hypertrophic glia cells containing fat droplets were present. Note the intense capillary hyperemia.

MORBID CHANGES OF THE CENTRAL NERVOUS SUBSTANCE ACCOMPANYING FATTY DEPOSITS IN GLIA CELLS OF FETUSES AND INFANTS OR PREDOMINATING IN CASES IN WHICH FATTY GLIA CELLS ARE ABSENT

When Virchow, in 1866-1867, reported on his observations, he was aware that the fatty glia cells signified only one aspect of the morbid changes caused by "congenital encephalitis." He described the proliferation and decay of glia cells, the swelling and disinte-

gration of nerve fibers, softening of the brain substance, overfilling of cerebral vessels which sometimes attained an apoplectic degree. As he, himself, in later polemics did not emphasize these properties of the disease which he discovered, they were completely neglected by investigators involved in the discussion. Nonetheless, it is a fact that even if we knew nothing about the presence of

Fig. 10. Scarifying birth traumatic softening foci in the subependymal white matter of the occipital lobe supplied by the lateral ventricular vein. Arrows indicate the foci.

fatty deposits in glia cells, we would still have to consider the brains of most infants who die in the paranatal period as diseased because of other changes of obvious significance. The areas affected by the appearance of fat droplets in glia cells are regularly characterized by a loss of the pre-myelin and myelin substances and of the basic substance of the nervous tissue, a change which causes the affected areas to display lighter color in histological sections, stained with hematoxylin, or, by Weigert's and Alzheimer-Mann's methods. (Fig. 8). The smaller a focus of this kind, the more marked the contrast to the surrounding areas, which are of greater density. This type of rarefaction of the cerebral substance is particularly marked in children 2 days to 10 days old. In infants who

die during the first three to five days of life, disintegrating nuclei of glia cells are very commonly found in those areas characterized by fatty deposits. In these regions of the central nervous system also, typical proliferative changes of glia cells are present: plasmatic hyperplasia of astrocytes, amitotic multiplication of the nuclei. (Fig. 1). These changes are characteristic of children who die after the second day of life. However, hypertrophic glia cells containing fat droplets in typical arrangement occur also in still-

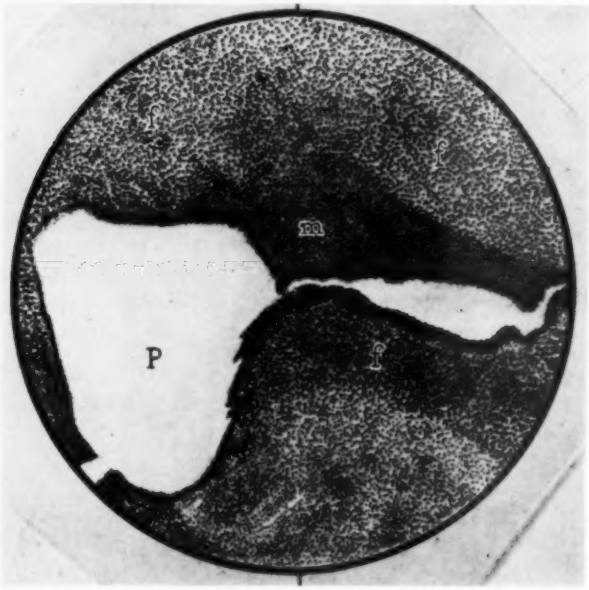

Fig. 11. Twelve-day-old dog, experimentally injured after birth. Extensive diffuse fatty deposits (black droplets) in the cerebral white matter. (*f*) fatty degeneration of the glia; (*m*) matrix; (*P*) large defect (porus) caused by the traumatic lesion.

born children who remained in the birth canal for a long time. (Fig. 1). Furthermore, in the areas of the typical fatty phenomena, debris and other products of diseased nerve fibers: ball-like and club-shaped structures, sometimes conglomerated in small groups, or, diffusely scattered, can be detected by searching carefully. (Fig. 3). No one doubted the pathological significance of minute necroses, and their consequential softening foci and scars of the cerebral white matter seen in almost every infant who died

between the second and thirtieth day following birth (Figs. 4, 5, 10). The most important and most frequent signs of a lesion of the central nervous system in newborn children, however, are hemorrhages which can be observed almost without exception in every stillborn child, or in infants who die a few days after birth. (Figs. 5, 6, 12, 13.). These hemorrhages are located in areas supplied

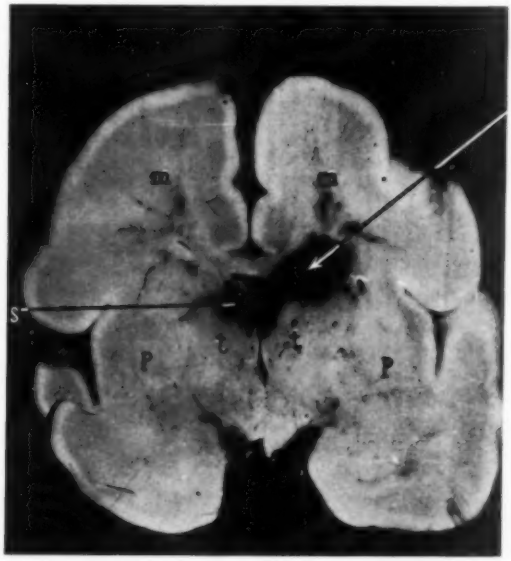

Fig. 12. Hemorrhage of the main stem of the left terminal vein, producing large subependymal hematoma. Hemorrhage of the vein of the septum pellucidum was present on the right side. Punctiform and strip-like hemorrhages affected the fronto-parietal white matter drained by the terminal veins.

These areas, in which circulatory disturbances are present, contained abundant fatty glia cells and debris of nerve fibers of a premature stillborn child. Arrow indicates the subependymal hematoma of the left hemisphere; (*s*) hemorrhage of the septum pellucidum; (*p*) putamen; (*t*) thalamus; (*m*) fronto-parietal white substance.

by the longitudinal sinus, the straight sinus, and primarily in the areas supplied by the branches of the Galenic vein. Hemorrhages originating from the stem of the terminal vein, as well as strip-like and punctiform extravasations involving the frontal, parietal and occipital cerebral white matter, which is supplied by the roots of the terminal vein and the lateral ventricular vein, are particularly characteristic. (Figs. 5, 6, 12, 13). In all these vascular segments, besides hemorrhages affecting the same parts of the central

nervous system, other circulatory disturbances, such as thrombosis and stasis, also are present, exerting the same pathogenic effect on the nerve tissue as hemorrhages.

In Rydberg's investigations, performed to verify the results obtained by the author, macroscopically visible intracranial hemorrhages were found in fifty-eight out of seventy-five newborn children. Macroscopic hemorrhages in the brain substance, or in the ventricular cavities were found in twenty-eight children. "Capillary bleedings or small extravasations, only detectable by microscopic examination, are very seldom absent in newborn children." Out of the seventy-five cases mentioned, Rydberg noted thirty-four instances of major cerebral symptoms. "In the majority of such cases, considerable intracranial bleedings are found. . . . Extensive intracranial bleedings are often found to be accompanied by an advanced softening process of the brain. . . . In six cases of major cerebral symptoms in which no intracranial bleedings of any importance were found, a considerable degenerative tissue change in the brain was observed." (Rydberg, l. c., p. 126). "Small necrotic areas are rather frequent in premature fetuses and are also seen, at times, in fully developed newborn infants." (Rydberg l. c., 65).

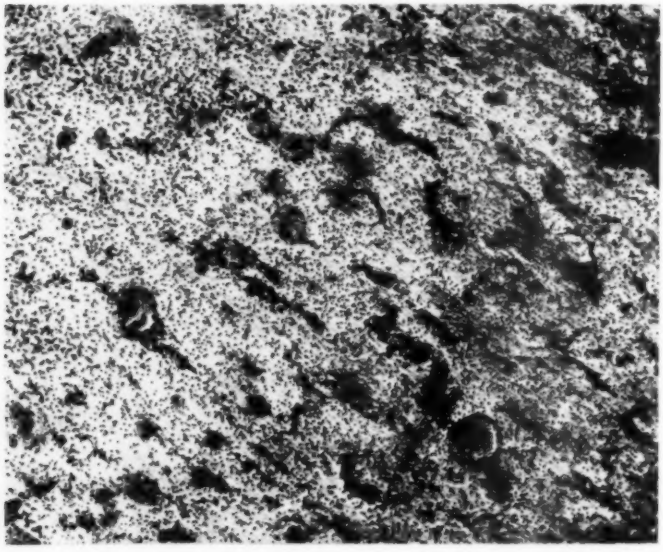

Fig. 13. Fresh capillary hemorrhages and intense diffuse fatty degeneration of the glia cells in the white matter of a 2-day-old, full term baby. Macroscopic inspection disclosed only hyperemia.

There can be no doubt about the fact that the fatty deposits in glial elements result from all these circulatory disturbances and signify the disintegration of the sheaths of the nerve fibers and of the basic substance of the cerebral tissue.

COMMENT

Reviewing the discussion on the significance of the fatty deposits in the nervous system of newborn children, the impression may be gained that we deal with unreconcilable differences in every sense. Actually, Wohlwill's opinion, namely, that the normal development of the central nervous system always is accompanied by fatty glia cells, appears incompatible with the results of the author. If this question of the embryological significance of fatty glia cells in the central nervous system of the newborn is of interest and perhaps of any value, then it seems that the real importance of the historic controversy lies in the decision whether the brains of newborn children displaying the fatty deposits are diseased or not. Indeed, this question can be considered as definitely answered. It is, from a practical, medical point of view, a matter of indifference whether we regard the brains of dead newborn children as diseased because certain microscopic fatty deposits are present, or, because hemorrhages are revealed. And hemorrhages, macroscopic and microscopic lesions are present in practically every stillborn child and in those who die a few days after birth. Also, it does not matter if the brain of a child, who survived the birth process only to die before reaching the thirtieth day of life, is declared diseased because certain fatty glia cells were detected microscopically, or, because softening foci were seen with the naked eye.

If we regard our problems from this point of view, then the refutation of Virchow's teaching by many investigators loses its acuity and becomes meaningless for all practical medical purposes. Thus we arrived at the most important result of all the investigations and discussions pursued during the last ninety years: *We may consider as an established fact that the brains of newborn children who die in the perinatal period, or during the first months of life, show morbid changes in the great majority of cases. This observation indicates new goals and new directions and, also, signifies a comprehensive anatomical basis for the pathology of the newborn.*

We mentioned that the term "encephalitis" was proposed by Virchow not because the disease was induced, in his opinion, by an infection transmitted in the uterus from the mother to the fetus, but simply because the morphological changes observed, concurred with the contemporary definition of the inflammation. The term "encephalitis" today, however, is reserved as applicable mainly to cerebral diseases caused by infections; even in those instances

where a brain condition is caused by an intoxication — that is, by lead — there is a tendency to substitute "encephalopathy" for "encephalitis." Thus, it seems inaccurate to designate brain damage, which for the most part was caused by paranatal circulatory disturbances, as an "encephalitis." A more exact name would be *"traumatic"* or *"anoxic paranatal encephalopathy of the newborn"*; or perhaps it would be preferable to refer to this condition as *"Virchow's disease of the newborn"*, as the name of this great medical discoverer and reformer hitherto has been linked only with the exceptional condition called "leontiasis ossium." Nevertheless, the term "encephalitis" originated by Virchow, could be used in a few cases, conforming to the modern meaning: as in those rare instances where congenital, intrauterine or paranatally acquired toxoplasmosis of the central nervous system is present (Wolf, Cowen and Paige); or in those even more exceptional cases, in which other infections, such as syphilis have been transmitted by way of the placenta. (Ref. Schleussing, 1935; Alpers and Patten, 1936; and Richter, 1936). It is interesting to note that after the discovery of the toxoplasmic encephalomyelitis by Wolf, Cowen and Paige, in 1939, this disease was recognized in some cases which had previously been published as Virchow's congenital encephalitis. (The observations described by Fischl, 1887; Wohlwill, 1921; DeLange, 1929; Richter, 1936; Müller, 1939, are assumed to belong to this group). Werthemann was able to recognize toxoplasmosis in a museum specimen, on display for many decades, as Virchow's congenital encephalitis.

Köhn, in 1952, expressed the opinion that the author had seen, described and illustrated the toxoplasma parasites as early as 1924, in his monograph on birth traumatic cerebral lesions of the newborn. Even if Köhn were right in his interpretation of the descriptions and illustrations he referred to, the author would like to emphasize that he had no knowledge of the parasitic nature of the structures observed. However, it is worthwhile, perhaps, to bear in mind the possibility of a combination of paranatal cerebral lesions of mechanical origin, and toxoplasmosis.

Softening processes, resembling in many aspects the changes characteristic of Virchow's encephalopathy, occur also in cases where the fetus' brain has been exposed to traumatic lesions during pregnancy. (Seitz) We observed, repeatedly, the same type of involvements following toxic and infectious influences affecting infants' brains soon after birth. (Ref. Hollinger).

Undoubtedly, lesions caused by intrauterine carbon monoxide intoxication also belong in this group. (Ref.: Maresch, Neubürger, Brander, and Hallervorden).

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IDIOPATHIC HYPERCALCEMIA IN INFANTS WITH FAILURE TO THRIVE. (Lancet, 2:110-115, July 17, 1954). This paper presents the clinical, chemical, and radiological features of 16 infants with idiopathic hypercalcemia and failure to thrive. It has been suggested that alkali medication might be a causal factor, but in the present series the syndrome developed in the absence of such therapy. Similarly there is no direct evidence to implicate previous pyelonephiritis as a causal agent, and the pyuria commonly found is probably secondary in nature. Smith stated that ingestion of increasing amounts of calcium led to larger fecal losses but also to surprising degrees of increased retention and that the degree of retention depended mostly on the amount of calcium in the infant's diet, which is four to six times as great with cow's milk as with human milk. Stearns observed that retention of calcium was much greater when vitamin D was added. The constant causal factor in the reported cases was a high calcium intake from early infancy, usually associated with a more than adequate amount of vitamin D in the diet. The author suggests that to prevent this condition breast feeding must be encouraged, and unnecessarily large doses of vitamin D discouraged, especially when vitamin-fortified dried milks are being used. A rational therapy should include a diet low in calcium and free from vitamin D. Spontaneous recovery can confidently be anticipated. The immediate prognosis is good: all infants survived.—*J.A.M.A.*

CLINICAL CONFERENCE

ST. LUKE'S HOSPITAL, NEW YORK

Meeting held April 8, 1958

Dr. J. Frederick Eagle, Jr., Director of Pediatrics, presiding

CONGENITAL HEART DISEASE IN A SEVEN-MONTH-OLD INFANT

Dr. Eagle: Today, our case presentation will be made by Dr. Stanley F. Piotrowski, Rotating Intern.

Dr. Piotrowski: D.N. is a seven-month-old male infant who has been known to have congenital heart disease since shortly after birth. There is a long family history of congenital anomalies on the maternal side of the family, including congenital heart disease, aplasia of the limbs, cerebral palsy, and visceral malrotation. The patient's older sibling died at the age of one year of congenital heart disease complicated by biliary atresia.

At the age of six weeks, he was referred to St. Luke's Hospital for evaluation and diagnosis of the heart lesion. He weighed five pounds and thirteen ounces which was only eleven ounces above his birth weight. Skin and sclerae were mildly icteric. The heart did not appear enlarged. There was a very loud systolic and diastolic, to-and-fro, machinery-like murmur heard best at the left third and fourth intercostal spaces. There was a definite right ventricular heave and a systolic thrill. The liver was 3 cm. below the right costal margin. The remainder of the physical examination was negative.

Laboratory examination revealed a normal hemogram and urinalysis. Serum bilirubin was 7 mg. percent; 6.4 mg. direct, 0.6 mg. indirect. Chest x-ray revealed some prominence of the pulmonary markings in both hilar regions. The size of the heart shadow was at the upper limits of normal. The EKG showed right ventricular preponderance which was considered normal for his age. It was felt that these findings were consistent with a diagnosis of a patent ductus arteriosus or a septal defect. Further diagnostic work-up was deferred until the child was older.

The child did not do very well at home, gaining about one pound the following month. He was readmitted at the age of ten weeks for a liver biopsy. The serum bilirubin was 4.5 mg., all direct. The liver biopsy revealed a mild degree of bile stasis, but bile ducts were present with patent lumina and there were occasional inspissated bile plugs scattered within some canaliculi. The EKG was unchanged.

It was still felt that the most likely cardiac diagnosis was patent ductus arteriosus and that the jaundice could be explained by inspissated bile ducts which could be expected to clear. He was discharged and the jaundice gradually cleared but his weight gain was very slow.

One month prior to admission, he developed pneumonia and subsequent heart failure which was treated in another hospital. Subsequently, he was transferred here. His appearance was quite grotesque. He was grossly underweight, practically marasmic, and his head, which actually was normal in size, looked hydrocephalic in relation to his puny body. There was no cyanosis or difference in color between the upper and lower extremities. There was no clubbing of fingers or toes. He weighed only eight pounds and was quite pale. The heart was grossly enlarged on physical examination. In the pulmonic area, there was a loud, harsh systolic murmur accompanied by a systolic thrust and no P2 was heard. There was a diastolic murmur heard lower down on the left sternal border in the fourth intercostal space. The liver was 4 cm. below the costal margin. The hemoglobin was 10.4 grams, WBC 18,000 with elevated polymorphonuclear cells. X-ray revealed a residual right consolidation in the right lung, and gross cardiac enlargement. The EKG continued to show right ventricular hypertrophy.

Shortly after admission he underwent a cardiac catheterization which will be described by Dr. A. L. Loomis Bell, Jr., Associate Attending Physician.

DR. BELL: This child was catheterized through the right femoral vein using local anesthesia. The arterial sample was taken from the right femoral artery. We were unable to get into the pulmonary artery although the tip of the catheter could be manipulated into the outflow tract of the right ventricle. The pressure in the right ventricle was very high, 105/9 mm. of mercury with a mean pressure of 40 mm. Normal values would be about 20/0 mm. of Hg. The average right atrial pressure of 10 mm. of mercury was also elevated and, in conjunction with a high diastolic pressure in the

right ventricle would indicate that the child has some right ventricular failure. The systemic pressure was 131/63 in the femoral artery with a mean of 94 and is within normal limits. In the presence of decreased lung markings, these findings are consistent with the diagnosis of pulmonic stenosis.

Oxygen content of blood sampled from the right ventricle shows a significant increase over samples from the inferior vena cava, and the right atrium. This would support a diagnosis of interventricular shunt from left to right. Since it is very easy to get through any atrial septal defect from the inferior vena cava, and since we probed this septum quite deliberately and could not demonstrate a defect, I think it is fairly safe to say that there is no interatrial communication. A femoral arterial blood sample revealed an oxygen saturation of 88.1%. This is somewhat in defiance of the clinical appearance of the child, who is not and never has been cyanotic. The absence of cyanosis might be accounted for by the fact that the child has a real degree of anemia. We calculated his hemoglobin to be 8.5 gm. (derived from the oxygen capacity of arterialized blood with an hematocrit of 26%).

To summarize, on the basis of these catheterization data, we have to say that this child has right ventricular hypertension, and that he probably has an interventricular communication with a primarily right to left shunting of blood. Pulmonic stenosis must be inferred.

We pulled the catheter back into the right auricle and then Dr. Hempel injected 10 cc. of 70% radio-opaque dye and an angiocardiogram was exposed. We would have liked to inject dye directly into the right ventricle but since we were quite sure there was no defect in the atrium, and since the right ventricle is an irritable area in which to leave the catheter, we injected into the auricle. Dr. Herbert F. Hempel, Director of Radiology, will interpret the angiocardiogram.

DR. HEMPEL: In this angiocardiogram, films were taken at approximately half second intervals from the time of injection of the radio-opaque dye. I will show you representative films. (See Figures 1-5).

On the basis of this angiocardiogram, we conclude that he has pulmonic stenosis and probably a ventricular septal defect.

DR. EAGLE: Dr Fitzpatrick, have we given you a diagnosis which you feel can be corrected surgically?

Fig. 1. This early film shows the radio-opaque medium entering the right ventricle and right auricle through a catheter which has been introduced into the right auricle via the vena cava.

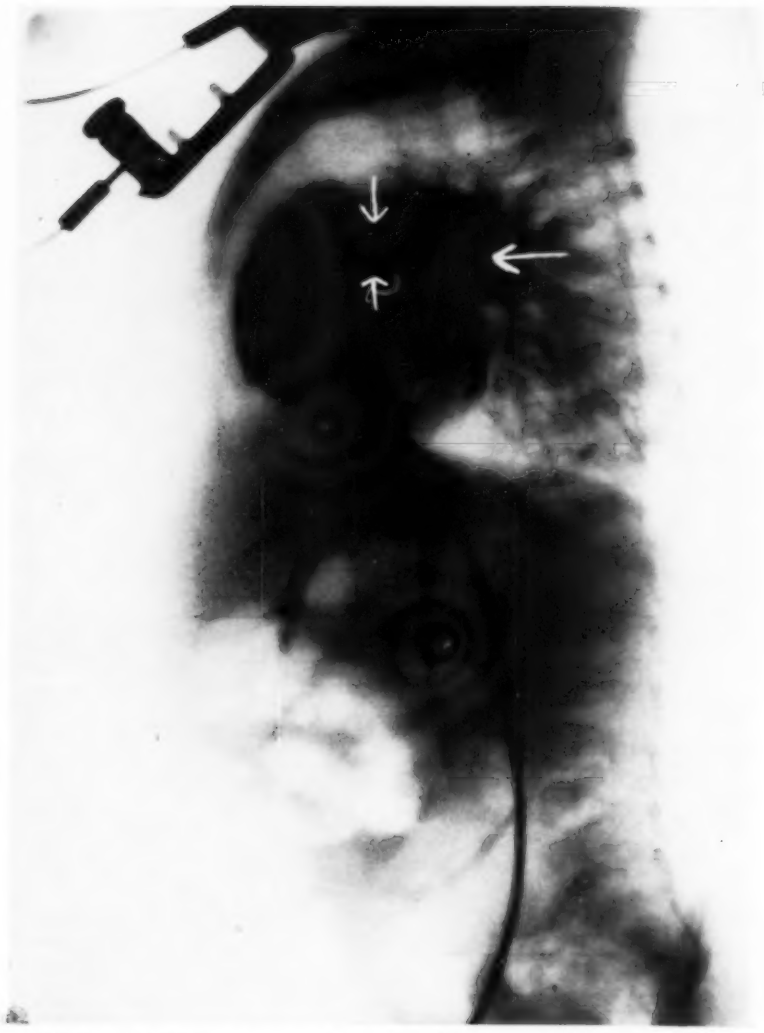

Fig. 2. A fraction of a second later the radio-opaque medium outlines the pulmonary circulation. The large horizontal arrow points out the post-stenotic dilatation of the pulmonary artery. The small vertical arrows indicate an area between the ventricle and the pulmonary artery where the outflow is narrowed. This is highly suggestive of pulmonic stenosis.

Fig. 3. Approximately 3½ seconds later the left auricle is opacified, presumably through the pulmonary circulation.

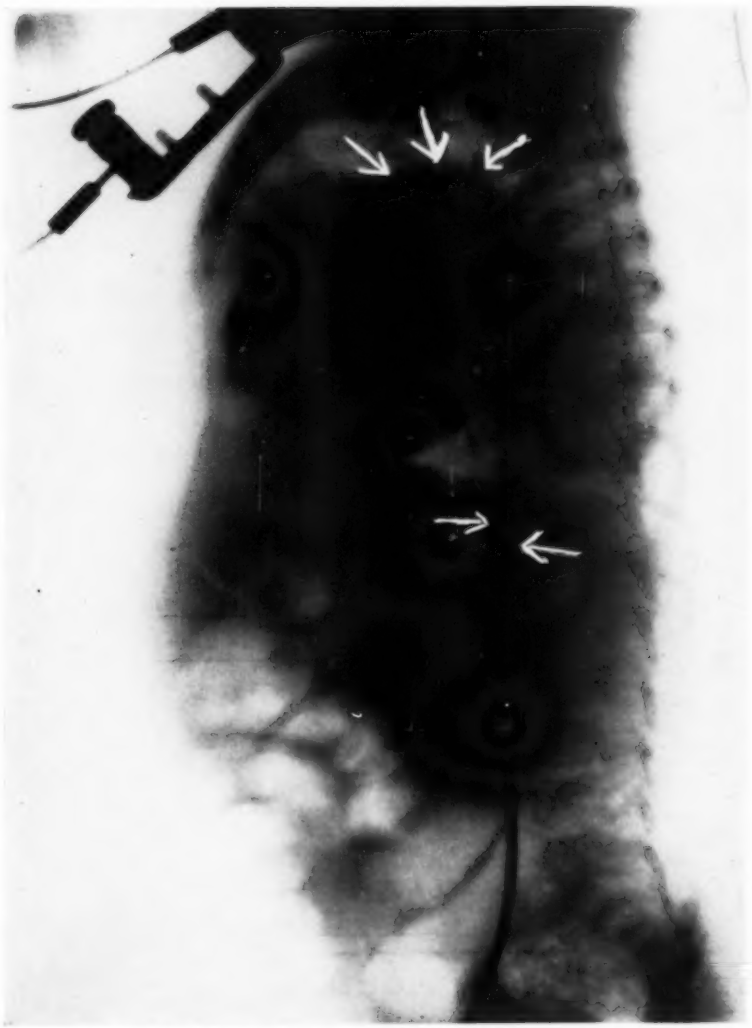

Fig. 4. This film shows opacification of both the thoracic and abdominal aorta.

Fig. 5. Approximately 3½ seconds later the radio-opaque medium persists in the left side of the heart and the aorta. There is probably in addition a re-opacification of the right side of the heart as indicated by the arrows.

Dr. High F. Fitzpatrick, Assistant Attending Surgeon: I would like to ask several questions. First, if this is pulmonic stenosis with an interventricular septal defect, is it a tetralogy of Fallot? Or could this be pulmonic stenosis with a low septal defect that would tend to eliminate the problem of the overriding aorta?

Dr. Hempel: This angiocardiogram does not suggest a diagnosis of tetralogy of Fallot. In a tetralogy we can graphically demonstrate simultaneous opacification of both sides of the heart and early aortic filling.

Dr. Fitzpatrick: Secondly, I would like to ask Dr. Bell what he thinks should be done.

Dr. Bell: I do not think that the angiocardiograms or the catheterization studies are typical of a tetralogy. I am bothered by the lack of clinical cyanosis since I am quite certain that he is unsaturated. If we believe these blood oxygen figures, there is a bi-directional shunt and the calculated pulmonary blood flow exceeds systemic flow. The angiocardiogram indicates that the pulmonary flow is not reduced. This has surgical implications because then one would not feel that a Blalock or a Potts procedure is indicated.

I do not believe that he has isolated pulmonic stenosis. I do not believe we can account for his clinical status, for the angiocardiographic findings, nor for the oxygen unsaturation without an admixture of venous blood somewhere, but frankly, I am not certain where the second defect is. I would think it more likely his pulmonic stenosis is valvular since there is no pulmonic second sound, because of the appearance of the angiocardiogram, and because of the pathway the catheter took before it fetched up in the outflow tract.

Dr. Elvira O. Ostlund, Associate Attending Pediatrician: Wouldn't you expect arterial saturation with isolated pulmonic stenosis?

Dr. Bell: Yes. However, he could be unsaturated on the basis of a primary lung lesion or from underventilation. In other words, if one assumes that the blood coming back to the pulmonary veins has a lowered oxygen content, we do not have to hypothecate any septal defect. I do not feel that there is enough atelectasis or pneumonia to account for the unsaturation, and since the catheterization was done under local anesthesia, I doubt that hypoventilation can explain the lowered arterial oxygen saturation.

DR. FITZPATRICK: I believe that this patient is a candidate for surgery. One possible procedure would be a shunting operation such as a Blalock procedure, but this does not appear indicated since pulmonary flow as evidenced by the angiocardiogram seems to be adequate. A second procedure would be alleviation of his pulmonic stenosis by means of a Brock procedure which can be done from above or below the valve. Such a procedure would ignore the ventricular septal defect and convert him into a so-called Eisenmenger's complex. This, in the long run, might do as much harm as good. Consequently, I think that we must be prepared to do an open-heart procedure using the heart-lung machine and plan to correct both the pulmonic stenosis and interventricular septal defect. To operate on a patient who weighs eight pounds, regardless of what one does is very risky, I would say, conservatively, the operative mortality was 70%. On the other hand, one has to weigh the operative risk against the prognosis without surgery, which I gather is even poorer. If there was any possibility that this child could be maintained and carried medically for another year, that course would be ideal. However, if the pediatricians feel that this is impossible, I believe we should try to correct the defect surgically at this time.

DR. BELL: I would suggest one further thought, that we make sure that there is no other organ or organ system involved which is contributing to this condition.

DR. EAGLE: This child at one time did have liver disease but he is now clinically free of jaundice. His liver biopsy showed some bile stasis, but was otherwise normal, and not consistent with neonatal hepatitis or cirrhosis. There is no evidence of other organ or system disease. Congenital heart disease is a common cause of failure of growth and development.

To summarize, we have presented a seven-month-old child in which the evidence points to pulmonic stenosis and a ventricular septal defect. The prognosis without surgery is thought to be exceedingly poor. The operation of choice is an open-heart procedure with correction of both the septal defect and the pulmonic stenosis. Although the operative mortality has been estimated at 70% in a patient of this kind, it is nonetheless felt that surgery offers a greater chance for survival than non-surgical management.

This article, written by one of Archives' senior editors, Dr. Philip M. Stimson, seems a most timely approach to the prevention of juvenile delinquency — an increasingly important subject, especially in our large cities. President of the Board of Directors of the Trail Blazer Camps (formerly Life Camps) for exceptionally underprivileged children and adolescents, Dr. Stimson is well versed in the problems besetting the teenager. We believe that this warm, informal article may be helpful to pediatricians in their approach to adolescent patients. J.F.L.

INTEGRITY IN THE ADOLESCENT*

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Many years ago I was doctor at a private summer camp where one of the big events of the summer was a series of baseball games with the boys of a neighboring rival camp. For our baseball coach a bush-league professional ballplayer was being tried and during an early inning in the first game when our team was at bat, our batter knocked a foul fly to the right of first base which their first baseman could probably have caught. But our coach called out, "Look out for the bicycle!" and their player stopped short and let the ball fall. There wasn't any bicycle.

That night at campfire, everybody was pretty quiet and one could sense that something was brewing. Suddenly our catcher blurted out, "If that's the kind of ball we're going to play, I don't want to play," and he spat at the fire as though there was a bad taste in his mouth. "Me too," "Me too" could be heard at once from others of the players — and that coach left camp the next day.

The following Sunday evening, ten or more of those older boys and I were sitting on some steps watching the sun go down behind the distant mountains and the lads talked about that episode. They hated it. To them it was bad taste, something dirty. At first, they did not think of it from the viewpoint of right or wrong — but as an act that went against the grain, that made them uncomfortable. They aired all the reasons why they didn't like it, the poor sportsmanship of it, the deception, how foul a game it would be if everybody did things like that, and they ended the evening much clearer in their minds about at least one aspect of trustworthiness — or shall I say, integrity.

I doubt if many of the adolescents we meet in social agency camps can be interested in acquiring integrity as such, especially

*Talk delivered at the 34th Annual Camp Directors Conference of the Palisades Interstate Park Commission at their banquet March 28, Bear Mountain Inn, on the general subject of Camping and Growth.

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if it means rigid uprightness like that of our nation's Puritan forefathers untempered with kindliness and graciousness. But trustworthiness or reliability can be understood — or even "good taste." One summer a young girl went to her mother and asked if she could go on a picnic with several of her young friends — without any older people. Her mother asked just who was in the group. At the first name the daughter gave, her mother exclaimed, "Oh, if he's going, everything will be quite all right. Of course you may go." Such was that lad's reputation for reliability and integrity.

How can we help our campers to develop reliability or uprightness, and in the first place to want to develop it. All too many youngsters today are not interested in what's right and what's wrong — but rather in "anything goes if you can get away with it."

There seem to be at least four methods of putting across to young people the meaning and desirability of trustworthiness. The first is by example. A father was scolding his daughter one day for having lied to him, when his wife called that he was wanted on the phone. He impatiently answered, "I can't come now, tell him I'm not home." The little girl looked at him with a very funny expression — which fortunately he was man enough to understand — and he apologized to the little girl. Both grew in integrity at that moment as they talked over that incident.

Dr. and Mrs. Ralph Bunche had dinner with us in our home one evening before going on to a concert by a blind colored singer in whom we were all interested. Dr. Bunche was immediately recognized as we entered the lobby and many people wanted his autograph and one young woman, an interview. He said to her he had not the time then but would see her afterwards. At the intermission he was again besieged so that at the end of the concert I suggested that we escape by a side door.

"Oh, no," he said gently. "I said I would meet that young lady." He valued his word. Of such is integrity, and I felt humbled by a great man. Campers meeting absolute reliability in their counselors and camp directors cannot help being impressed.

For the second method, certain attitudes of the adults in a camp towards the campers are helpful towards establishing a right way of life. The value of praise and appreciation of some act of reliability is increased if the approval is given in the presence of several persons. It spurs the ambition of all the hearers. But reproof of a youngster is for him alone and should not be over-

heard by anyone — lest he "lose face" both with himself and the others.

Trustworthiness includes responsibility and just as adults are held responsible for what they do, so should campers be. Even as a man who dents another man's car must make it right, so also a camper who steals someone else's carefully picked can of blueberries should make recompense with fresher, better berries. Instead of punishment, responsibility for the consequences of a misdeed makes sense to children. A small patient of mine clipped his friend on the head with a metal toy causing bleeding. Instead of spanking him, his mother had him make a present to his friend of his newest plaything and each morning for a week had him go to the door of his friend's home and inquire if the cut was healing well. That, for him, was learning what an adult might do.

Another attitude counselors might take is to say only what is kindly and gracious. Grace and courtesy are catching. A factory worker went to the pastor of a church in Ossining and said he wanted to join the church. The minister asked him why and he answered that his boss was the finest man and had the nicest way with people of any man he had ever known and was a member of that church and he thought that maybe if he joined the church he could learn to be a little like his boss.

The third method of arousing interest in integrity is by campfires or other twilight discussions. Is it ever right to tell a lie? What is cheating? What is good taste? A particular situation or problem can be presented and the arguments for and against a course of action be enumerated and then judged. For example, a youngster finds a purse in the street, what should he do with it and why? Incidentally, on the Floating Hospital when a thousand mothers and children are taking the trip it is a usual thing for lost articles to be turned in to the superintendent, perhaps because occasionally such an act is publicized on the loud speaker system. To paraphrase a proverb—"One good deed, when heard about, begets another". But on the other hand, doing a good turn for someone is made better by not being found out. Why this can be so is another potential subject for a campfire discussion and there are many such which might well contribute to a better concept of integrity and a greater desire for its attainment.

The fourth way to crystalize a concept of integrity is by explanation or actual instruction. Some twenty-five years ago the famous preacher, Rev. Dr. Harry Emerson Fosdick, preached a sermon on "Six Ways of Telling Right from Wrong". The fol-

lowing points are founded on that sermon but from frequent usage over the intervening years, probably no longer closely resemble his inspiring words. But his ideas are applicable to each one of us. Almost any adolescent can be led to understand and appreciate any of the points.

A first point is—"Does it have to be concealed?" "Is it sneaky?" There are so many situations where this applies that an illustration is hardly necessary. If a politician faces a deal he would not want publicized in the papers, his course should be clear. To be able to live without fear of being revealed at any weak point is one part of trustworthiness.

A second way of telling right from wrong is "what does this lead to?" Almost always there will be lying, often shame and regret, or humiliation—also loss of a good reputation—possibly even loss of a job. A hospital technician wrote on a patient's chart the imaginary report of a blood count she should have made but for laziness or some such reason, didn't. The patient said no one had pricked her finger for a blood count and at once, all that technician's work became suspected as inaccurate and untrustworthy.

The third way is "Does this spill over on somebody else?"—a husband or wife, a parent, children, anybody, sometimes almost everybody? A trusted doctor has several drinks one evening. He has an accident and is called a drunken driver. It gets in the papers, his wife and children suffer, his patients' confidence in him is shaken, and perhaps even people were injured in the accident.

Or a star athlete in a high school is found one night with stolen goods. It is not difficult to imagine all the people affected by such a discovery and listing them might be an interesting study for a campfire group. Dwight L. Moody said that "Character is what a man is in the dark".

The fourth point is "Is this a privilege I'm taking for myself alone, or would it be all right if everybody did this?" Is it bad sportsmanship like what the baseball coach did?—or like crowding in at the head of a line?

The next point is somewhat different. "Would the people I admire most do a thing of this sort?" We all know individuals —a preacher, a teacher, a doctor, a camp counselor, whom we couldn't conceive doing such a thing as we had thought of doing. Unfortunately, for many of our campers, it won't be a parent they can think of that way. It might well be a social worker, or

a counselor who has "sold himself" or herself to the camper and whose absolute reliability and trust keeps the youngster going straight. I believe it was Emerson who wrote: "What you are speaks so loud we cannot hear what you say."

What his conscience tells an adolescent is not necessarily right. Some have no consciences. Some, a warped conscience like the New England Puritans who persecuted witches. Some won't obey their consciences anyway, but there are still two influences that can stir a lad to better things and better ways. A youth whose behavior is a burden to his family, to his teachers, even to his associates and above all to himself, comes to admire greatly a scout leader, or a social worker, or even falls in love with a nice girl who exclaims to him—"Don't be silly" and more is accomplished than all the scolding, the threatening, and the nagging could possibly do.

No one wants to appear silly. In a baseball training camp eccentricities are laughed out of a rookie by ridicule. In younger people ridicule can be too rough a procedure—but a simple "Why be silly" might accomplish wonders.

The other technic is to appeal to a young person's "good taste" —good taste first in little things—in manners, as at a table, in dress, in speech, then in books, in music, then finally in relations with others, in morals, in love affairs.

To many, good taste as such is understandable and appealing. It is a characteristic we admire in others and which we would like others to admire in us. To say of a girl, she shows "good taste in her clothes" or "She's always in such good taste" are both nice compliments. Or of a man, "His stories are never in bad taste" or "He has too much common sense, too much good taste ever to do what you are suggesting" are even better compliments. Such people have good taste about their living and instinctively feel the difference between fair and foul. Good taste can be acquired even in a camp.

The following experience I once had illustrates many of the points I have been discussing although it involves a slightly older girl than the usual camper. One Saturday afternoon I was working alone in my office preparing a lecture for Monday when the doorbell rang. A pretty little blond was there, and asked if she might speak with me. She had been walking by and saw my name in the window but didn't know me. I showed her to a chair across the desk from me, and asked what I could do for her. She wanted to know about birth control. I said tell me about your man. So

presently I learned he was 25, an actor, and she had known him six weeks. Her parents had not met him. She was 17. Her home was in the mid-west, she had been in New York City nearly three months, she was living at a certain Club for girls. I knew of this club and its none too careful regulations so I suddenly said to her, "You're not planning to marry this man, are you, but to spend weekends with him"—and she blurted out, "I don't see why I shouldn't—all the girls are doing it". So we talked along and we first agreed that it didn't matter to her what the other girls were doing or at least were saying they were doing—but what did concern us was what might this lead to, what were all the possible consequences to her of her plans. We listed them together—First, pregnancy, which would be awful. Second, venereal disease, of which she had never heard—but she did then. Third, remorse and shame, especially if her parents ever heard. How would it affect them? Fourth, he'd leave her for another girl. "Oh no, he wouldn't do that"—"Do you really think you are his first girl? What happened to that first girl, or the second, or the third?" So the fifth point was promiscuity which usually starts as she would be starting. Finally, you might even marry him—but was a man who would suggest an illicit love affair to her the kind of man she had always imagined as her beau ideal—the kind she would want for the father of her children? Was there any other possible outcome? We could think of none. So I said: "Don't be silly! You obviously have good taste in dress, in manners,—do above all, have good taste in love; keep yourself clean until you marry the right man—and go back and pass on to some other girl what you in your innocence have learned for the first time this afternoon. Incidentally, do you want to know about birth control now?" "No, maybe not".

A week later I tried to call her at the club but she had moved. I hope she had gone home, but I never learned.

Dr. Fosdick once worded such a situation in a way I wish I had known for that girl. He said in a sermon apropos of good taste: "The love side of your life can be the most beautiful thing in your experience or it can be the most ugly. Which will you have?"

So far, this talk has been largely from an ethical viewpoint. It would not be complete without the following episode: A week ago tonight my wife turned on the television and chanced to catch a view of a dressing room bench on which Bud Palmer was interviewing the negro fighter, Virgil Akins. He had just won at

Madison Square Garden and was still dishevelled and soaking with perspiration. The conversation went something like this. Mr. Palmer was talking and asked Mr. Akins: "After the knock-out and in all the tumult in the ring, I noticed that you went and sat down quietly in your corner and started reading the Bible. How come?"

"Well Mr. Palmer," the boxer replied, "I never could do anything right and I was all mixed up and one day I started reading the Bible and I read in Matthew "But seek ye first the kingdom of God and his righteousness and all these things will be added unto you". Now I read the Bible a lot and when I'm up against something—I just put my hand in God's hand and do my best."

As the prizefighter and his manager moved away, Mr. Palmer made the remark—"What a wonderful demonstration of Faith".

What all this boils down to is—if each person—man, woman, or child, counselor or camper, teacher or student, parent or offspring, regulated his own life to do the right as he or she best understood it and thus lived true to his best self, then several things would happen. First, he would never need to fear being found out, or to dread the consequences,—second, he would affect others' lives by his example of right living, and third, this would be a better world for us all. In Hamlet, Polonius says "And this above all: to thine own self be true and it must follow as the night the day thou can'st not then be false to any man".

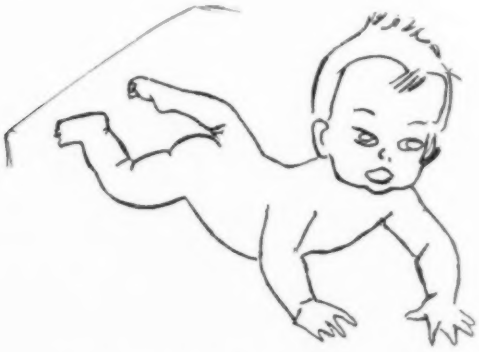
OXALOSIS: A NEW METABOLIC DISEASE OF THE "STORAGE" TYPE. G. DeToni, P. Durand and C. Rosso. (Minerva pediat., 9:623-637, June 1957). The authors report on an 11⅓-year-old child, a dwarf, with ichthyosis, horse-shoe kidney, an nephrocalcinosis, combined with several biochemical and functional signs characteristic of classic renal insufficiency, hyperchloremic renal acidosis, and severely impaired ammoniogenesis. The child did not respond to any of the various treatments and died after a progressive worsening of the symptoms of renal failure. The diagnosis of oxalosis was made on the basis of the histochemical examination, which revealed crystals of calcium oxalate in the kidneys and in the cartilage of the bones.—*J.A.M.A.*

PROPHYLAXIS FOR FOOT EVERSION IN INFANTS

ROBERT COHEN, M.D.*

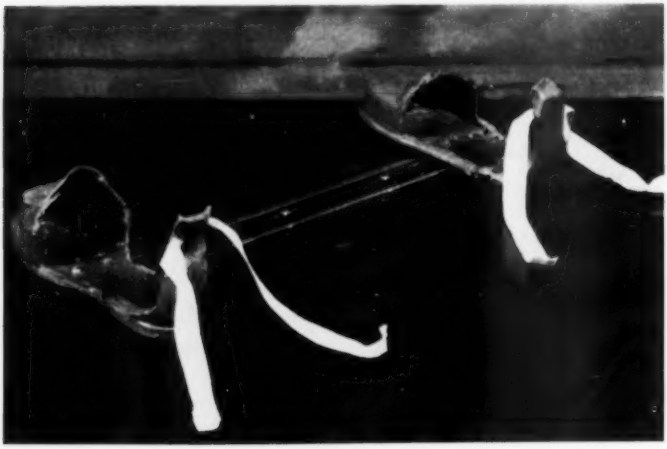
Bakersfield, Calif.

The average infant lying on his stomach presents the ideal position for nasal discharge, regurgitation and burping. Yet this same position is far from ideal when it comes to his feet as for



Eversion of feet due to positional sleeping

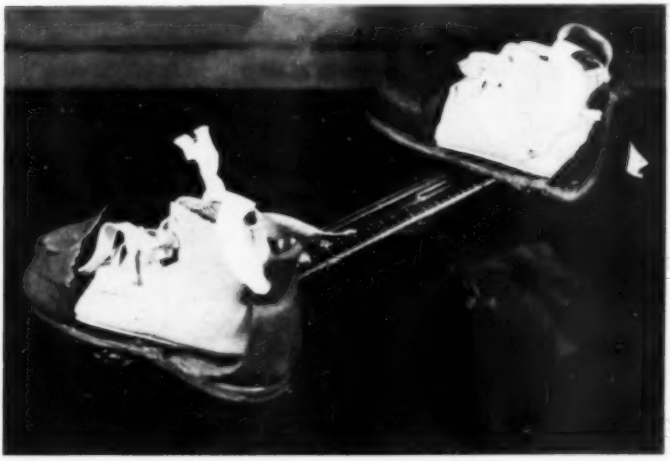
the most part they will be bilaterally everted to ninety degrees. A contented baby, who is not too active in his sleep will be found,



Plastic shells ready for insertion of shoes

almost always, in this position of foot eversion. As a result, a goodly number will subsequently need orthopedic correction of some sort.

A plastic shoe shell on a plastic rule, set at a ninety degree angle, was devised so that the shell can be slipped on over the infant's shoes, and he can sleep wearing this light foot-straightener. The portion of plastic from the achillis heel area is made flexible so that the shod foot can be inserted into the shell, then buckled or tied on, and on awakening, it is a simple matter to slip the shoes out and resume normal free play of the feet. Actually, this instrument is similar to the Dennis-Browne splint, but differs in that it has the plastic shoe shells into which the infant's shoes



Infant's shoes inserted in shells

are inserted. As previously mentioned, these shells are fixed at a ninety degree angle and the band joining both shoes is a plastic ruler. It is much lighter in weight, and more economical than the splint.

This device is not meant to replace the Dennis-Browne splint, but to assist the infant in the first three to four months of life, when not too agile, he lies contentedly in one position.

* Attending Pediatrician at Kern General Hospital, Bakersfield, California.

DEPARTMENT OF ABSTRACTS

Edited by

MICHAEL A. BRESCIA, M.D., NEW YORK

PETERSDORF, R. G.; CURTIN, J. A.; HOEPRICH, P. D.; PEELER, R. N. AND BENNETT, I. L., JR.: A STUDY OF ANTIBIOTIC PROPHYLAXIS IN UNCONSCIOUS PATIENTS. (New England Journal of Medicine, 257:1001, Nov. 21, 1957).

Of seventy-two patients, with no overt infection, thirty-two were treated prohylactically with penicillin and streptomycin or tetracycline, and ten with sulfisoxazole or nitrofurantoin, and no antimicrobial prophylaxis was administered to the remaining thirty. The mortality rate was not influenced by antibiotics; however, in 45 per cent of the prophylactically treated group, pulmonary complications developed, whereas pneumonitis occurred in only 15 per cent of the controls. Seven of the treated group had cutaneous infections with hemolytic Micrococcus pyogenes var. aureus (Staphylococcus aureus), and two died with bacteremias due to gram-negative organisms. These complications did not occur in patients from whom antibiotics were withheld. Chemoprophylaxis did not reduce the micrococcal-carrier rates, and strains isolated from the treated group were more resistant to antibiotics than those cultured from controls. There was, in addition, a replacement of the nasopharyngeal flora by gram-negative rods. Routine administration of antibiotics neither prevented nor ameliorated infection of the bladder in patients with indwelling urethral catheters. Although the resistance of the bacteria in the urine did not increase during treatment, strains of other species even more refactory to antimicrobial therapy regularly appeared. These data support the thesis that prophylactic antibiotic therapy is of no benefit, and is distinctly hazardous in unconscious patients.

AUTHORS' SUMMARY

PHIBBS, B.; BECKER, D.; LOWE, C. R.; HOLMES, R.; FOWLER, R.; SCOTT, O. K.; ROBERTS, K.; WATSON, W. AND MALOTT, R.: THE CASPER PROJECT—AN ENFORCED MASS-CULTURE STREPTOCOCCIC CONTROL PROGRAM. (Journal American Medical Association, 166:1113, March 8, 1958).

For three years, an enforced mass-culture program for detection and treatment of streptococcic desease has been under way in the

primary schools of Casper, Wyoming. The procedure consists of daily inspection of all "symptomatic" children with culture of suspicious individuals, and exclusion of those found to be infected with beta-hemolytic streptococci. Infected individuals are allowed to return to school only after adequate antibiotic therapy has been initiated. Introduction of this type of control produces a significant fall in incidence of streptococcic infection in the controlled population. Interruption of the program—as during the holidays—is followed by a rise in incidence of streptococcic infection. Reinstitution of control measures is followed by another drop in incidence. Family follow-up in cases of repeated infection discloses carriers in the family in 31 per cent of the families studied. In a small group of children (497), the incidence of streptococcic infection of symptomatic individuals was found to be significantly higher than in those who were asymptomatic. However, the group studied in this connection was too small to permit definite conclusions to be drawn. Enforced treatment or exclusion of school children infected with Streptococci is both practicable and consistent with policy on other infectious diseases. This type of program appears to lower the incidence of new cases of rheumatic fever in the controlled groups to a highly significant degree. It seems likely that this program has been effective in lowering the incidence of new cases of acute nephritis in the controlled group. As an educational effort, this type of mass-culture program is extraordinarily efficacious. Inexpensive mass-culture methods evolved in this program, together with the use of volunteer help, made the project practical in economic terms. AUTHORS' SUMMARY

RAINER, E. H. AND BULLOUGH, J.: RESPIRATORY AND CARDIAC ARREST DURING ANESTHESIA IN CHILDREN. (British Medical Journal, 5052:1024, Nov. 2, 1957).

A new method of resuscitation after respiratory and circulatory arrest is described which has been successfully employed on eight children. There has not been one single fatality. The method consists basically in intermittently flexing and extending the whole body, to which may be added positive-pressure inflation of the lungs with oxygen. It is believed that the method represents sound and effective approach to dealing with cardiac arrest in children. Though it has been used by us only in the operating theatre, we think it may have wider applications. It is more rapidly and more easily applied than other methods AUTHORS' SUMMARY

LITCHFIELD, H. R.: CLINICAL EVALUATION OF MEPROBAMATE IN DISTURBED AND PREPSYCHOTIC CHILDREN. (Annals New York Academy of Sciences, 67:828, May 9, 1957).

Meprobamate is the drug of choice in the treatment of a wide variety of children of all ages manifesting prominent symptoms of anxiety and tension, with or without organic disease, who are seen and treated primarily by the practicing pediatrician on an ambulatory outpatient basis. The drug appears to be of definite value in the control of petit mal epilepsy. It appears to be essentially nontoxic. Because of its selective action in sparing the higher cortical centers, it produces a tranquilizing effect without dulling of consciousness, disturbance of the mental faculties or hypnosis. In no instance, either in young or older children, did the drug retard their mental abilities. M.A.B.

SANTESSON, G.: ASPECTS OF SALT FLUORIDATION. (Northwest Medicine, 57:39, Jan. 1958).

A short review is given of the advantages and possibilities of salt fluoridation, and reference is made to the present (since 1956) distribution of artificially fluoridated salt on the Swiss market. I also advance the opinion that a complex fluoride less toxic than sodium fluoride, yet equally cariostatic—viz., sodium monofluorophosphate—may be especially suitable for salt fluoridation. Two different salt compositions, one containing 100 mg. F/Kgm. salt as NaF, the other 100 mg. F/Kgm. as Na_2PO_3F, were investigated. One per cent solutions of these salt compositions in distilled water (containing 1 ppm. F) were shaken for varying time-intervals with powdered human enamel. The absorption of fluorine from the salt solutions, as determined, was found to be almost identical for both salt compositions, although Na_2PO_3F under the given conditions yields the essentially stable, complex FPO_3-ion and not free ionic fluorine. AUTHOR'S SUMMARY

EICHENWALD, H. F.; ABABIO, A.; ARKY, A. M. AND HARTMAN, A. P.: EPIDEMIC DIARRHEA IN PREMATURE AND OLDER INFANTS CAUSED BY ECHO VIRUS TYPE 18. (Journal American Medical Association, 166:1563, March 29, 1958).

Evidence has been presented linking ECHO virus type 18 to two separate but closely related outbreaks of diarrhea in premature and older full-term infants. This represents the first instance in which a virus isolatable by laboratory methods has been shown to be a cause of an outbreak of epidemic diarrhea.

AUTHORS' SUMMARY

Coming Events . . .

Announcement is made by Doctor E. L. Denton, Secretary General, that the IX International Congress of Paediatrics will be held July 19-25, 1959 in Montreal, Canada. Under the auspices of the International Paediatric Association, and the invitation of the Government of Canada and the Canadian Paediatric Society, the scientific program is planned to embrace the broadest aspects of the problems of child care and will include plenary sessions, panel discussions and a display of scientific exhibits. Simultaneous interpretation in the official languages—English, French and Spanish—will be employed for all plenary session. Worldwide distribution of the preliminary program and registration forms will be made to pediatricians in a few months.

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Courses . . . The tenth annual summer clinic of The Children's Hospital in Denver, Colorado, will be held June 18-20, 1958. The course will present recent advances in medical knowledge appropriate to practice, and is designed for all physicians dedicated to infant and child care; emphasis will be on early recognition of disease, common problems in their management, at the same time outlining successful programs of therapy. Specific information may be obtained by writing the Chairman, Summer Clinic Committee, Children's Hospital, Denver 18, Colorado.

The Second Oklahoma Colloquy on Advances in Medicine will be held on November 12, 13, 14 and 15. It will be devoted to Arthritis and Related Disorders and is under the joint sponsorship of the Department of Medicine, University of Oklahoma, the Division of Postgraduate Education, Geigy Pharmaceuticals, Wyeth Laboratories, The Upjohn Company, Pfizer Laboratories, and Schering Corporation.

Short *refresher courses* for practitioners, pediatricians and clinical pathologists will be offered at the Children's Hospital of Philadelphia, in: Pediatric Advances, May 26-30; Practical Pediatric Hematology, June 2-4; Hemolytic Disease of the Newborn, June 5-6. Dr. Irving J. Wolman, 1740 Bainbridge Street, Philadelphia, Pa., may be addressed for information.

EVERY LISTED PEDIATRIC SPECIALIST

was questioned by an independent research organization about an article published in the Archives of Pediatrics. These specialists were asked whether they agreed with the reprint material.

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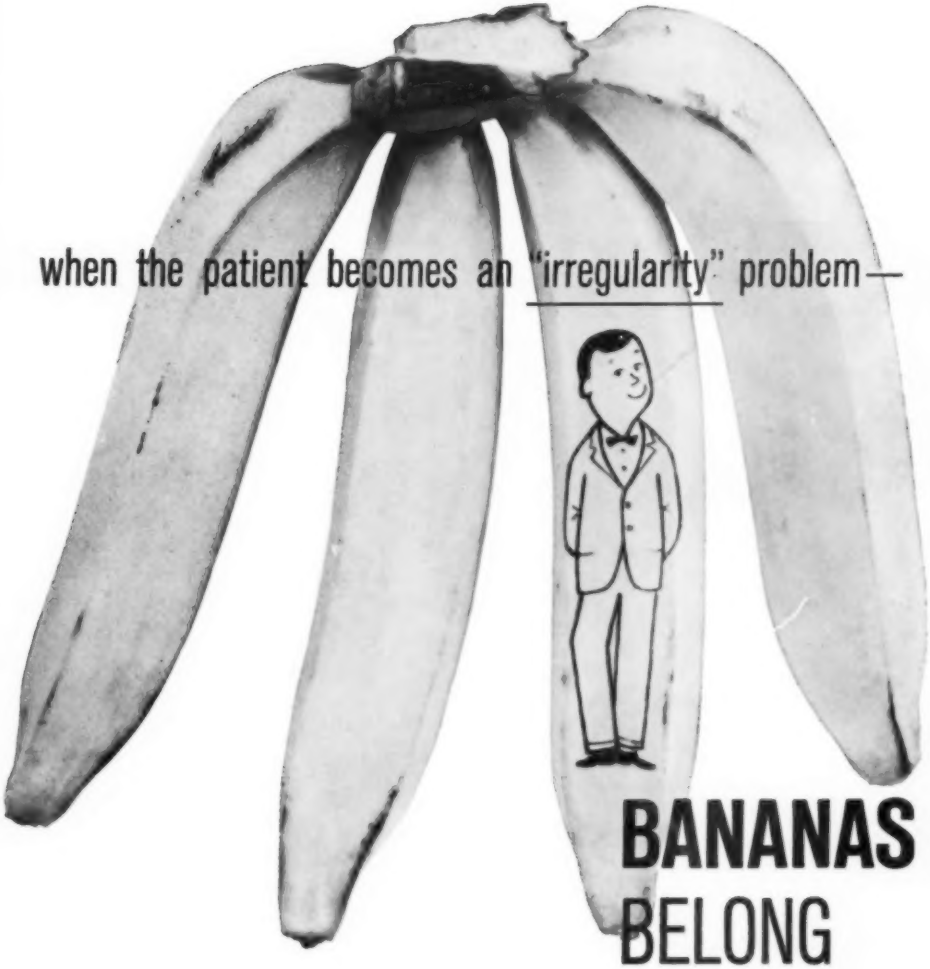

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1. New and Unused Therapeutics Committee, Am. Coll. Allergists: Interim Report at Thirteenth Annual Congress, Mar. 20-22, 1957, Chicago, Ill., Ann. Allergy, to be published. 2. von Schlichtegroll, A.: Arzneimittel-Forsch. 7:237 (Apr.) 1957. 3. Spielman, A. D.: New York J. Med. 57:3329 (Oct. 15) 1957.
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